Twenty-Third Annual Meeting
New York City, May 29-June 2, 1957

VOLUME XXXI NUMBER 3

DISEASES

of the

CHEST

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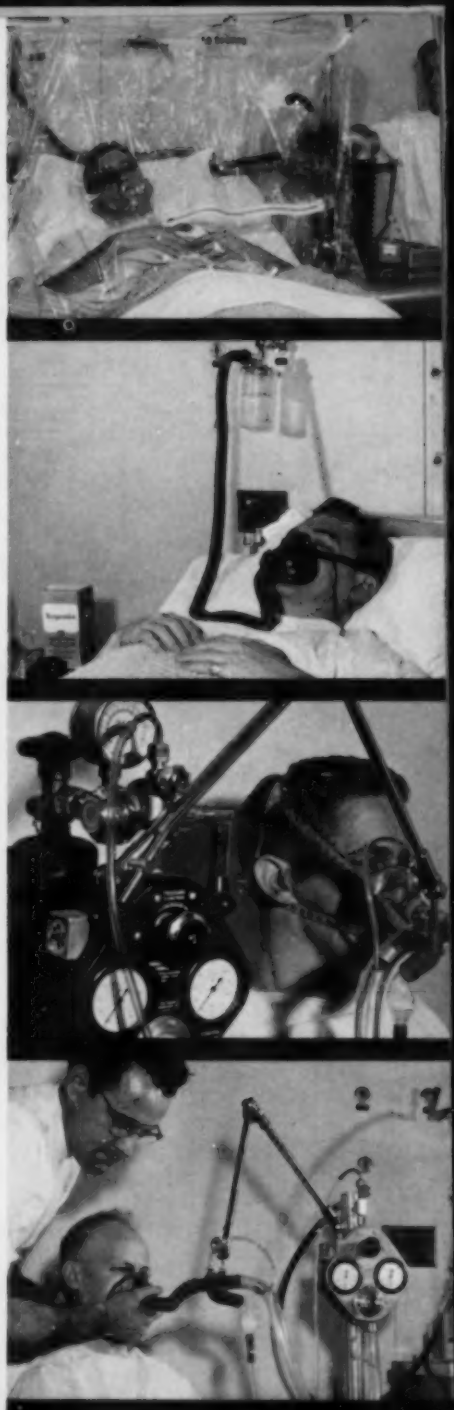
1. Levine, E. R., 1956, paper accepted for publication in *Diseases of the Chest*.



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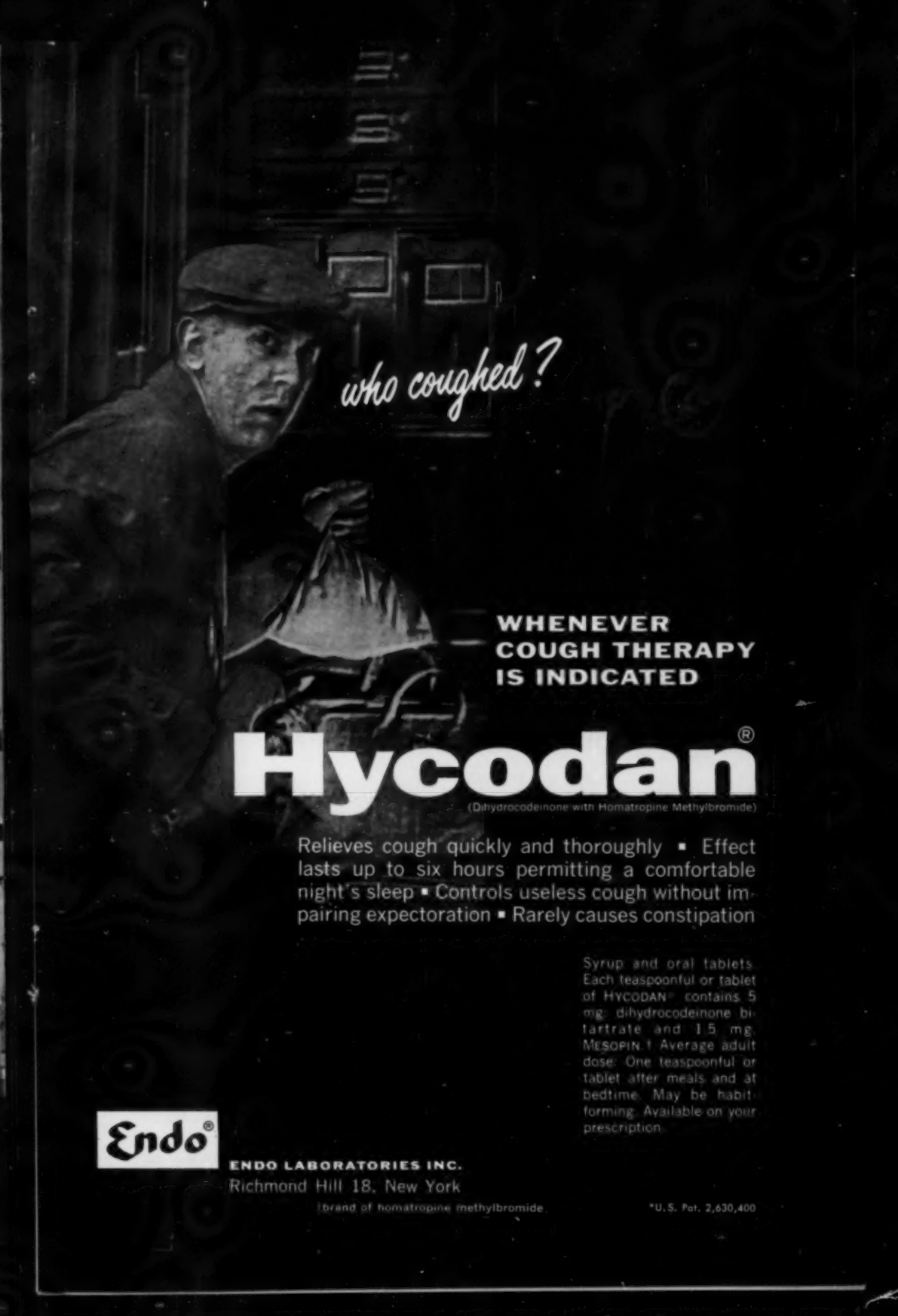

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Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.

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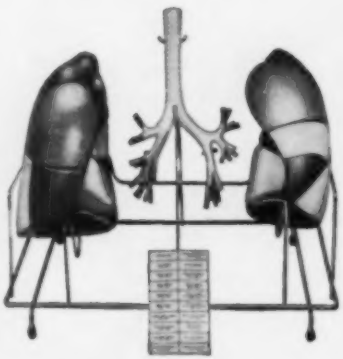

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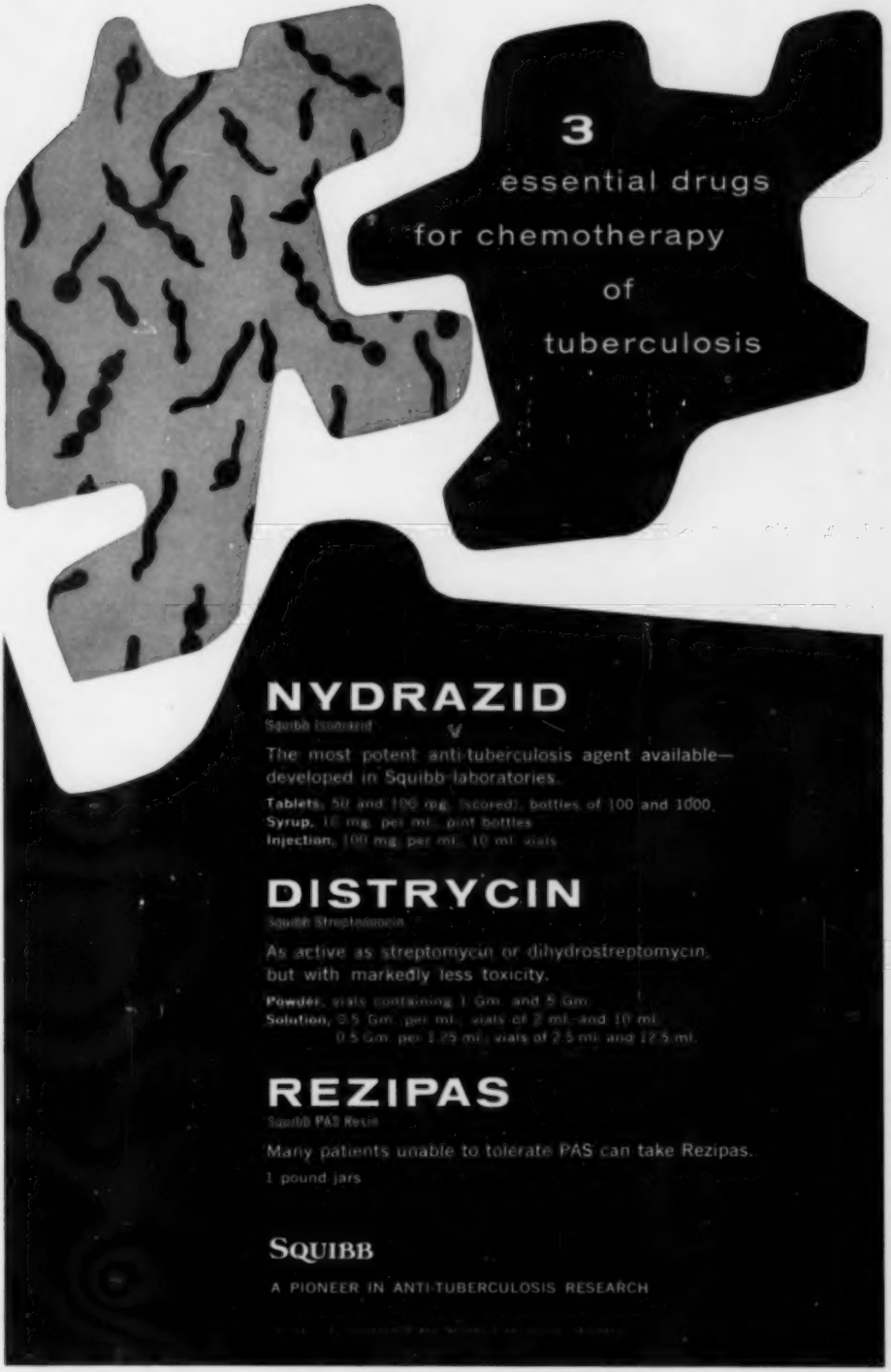
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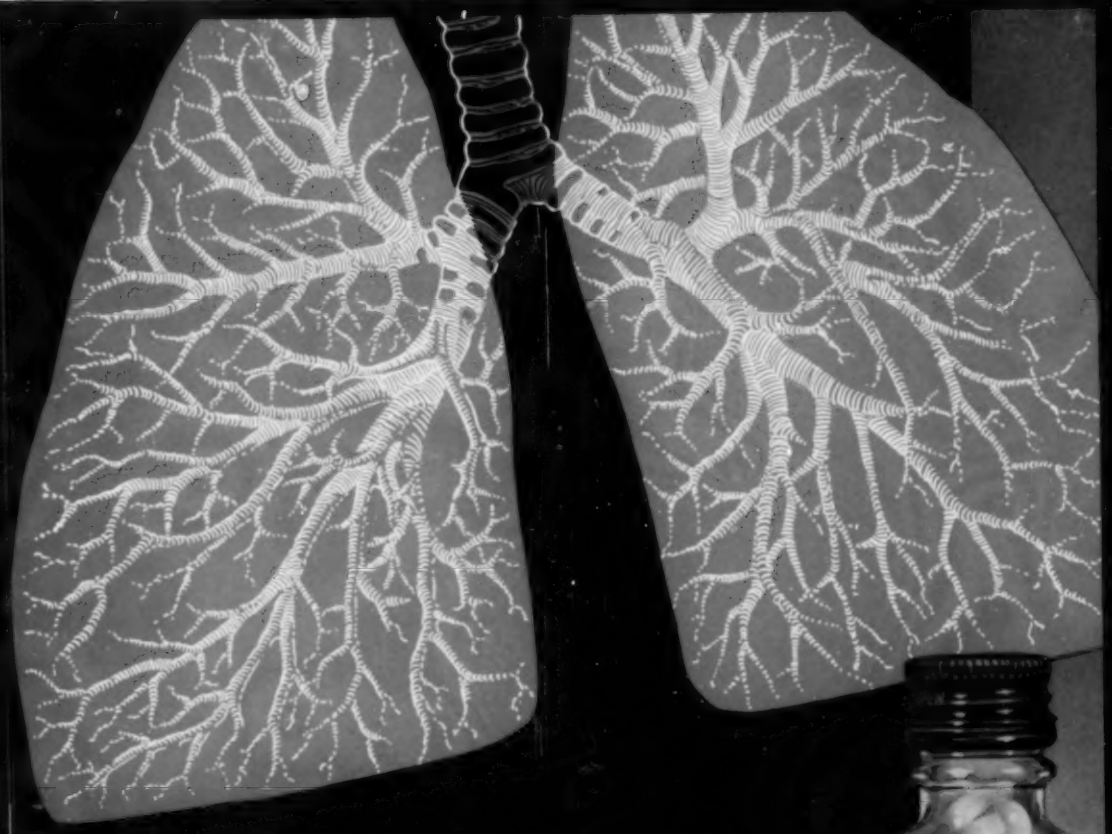

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Bellevue-Stratford Hotel, Philadelphia, April 1-5

CHAPTER MEETINGS

Illinois Chapter, Chicago, March 19

New England States Chapter, Boston, March 20

New Jersey Chapter, Newark, March 27

Missouri Chapter, Kansas City, March 31

Tennessee Chapter, Nashville, April 10

Arizona Chapter, Yuma, April 12

Alabama Chapter, Mobile, April 17

California Chapter, Los Angeles, April 27

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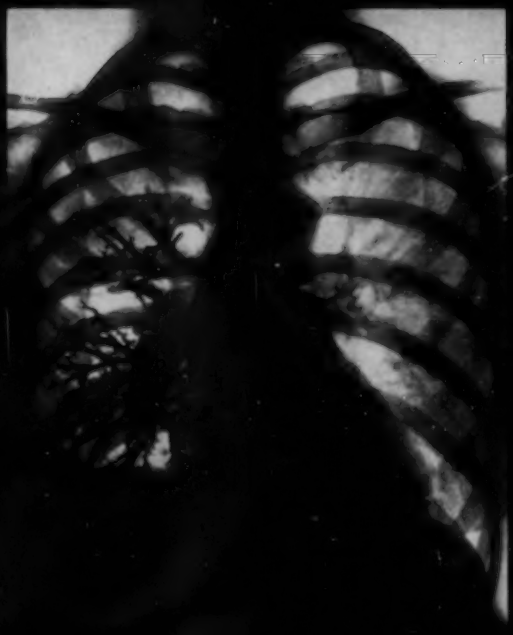

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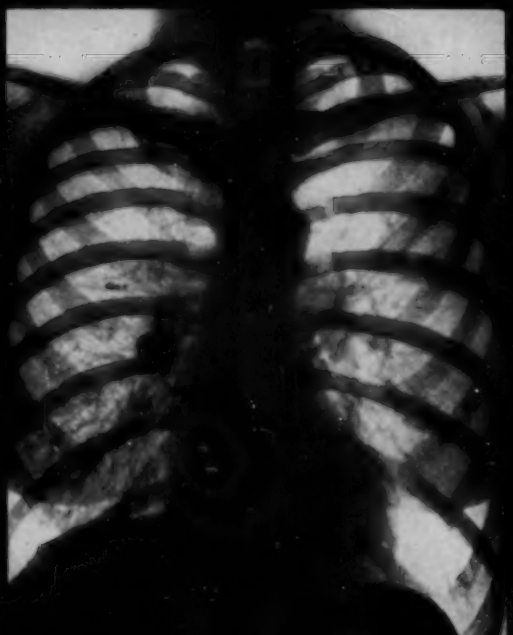

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1. Burrascano, J. J.: Sea View Hosp. Bull. *15*:149 (July) 1955.

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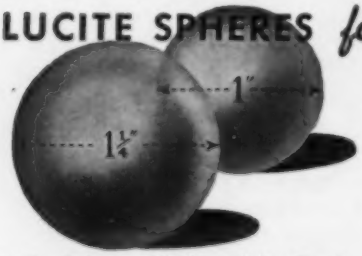

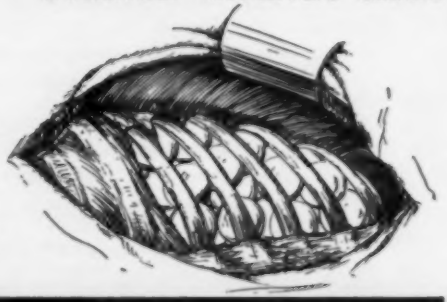

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1. Blanchard, K., and Ford, R. A.: Journal-Lancet 74:443, 1954.
2. Blanchard, K., and Ford, R. A.: Rocky Mt. M. J. 52:278, 1955. 3. Cass, L. J., and Frederik, W. S.: Am. Pract. & Dig. Treat. 2:844, 1951.

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[1]Dr. Samuel Phillips: *Calcium Benzoyl PAS*, Paper presented at 15th VA-Army-Navy Conference on Chemotherapy of Tuberculosis, St. Louis, Missouri, February 6-9, 1956.

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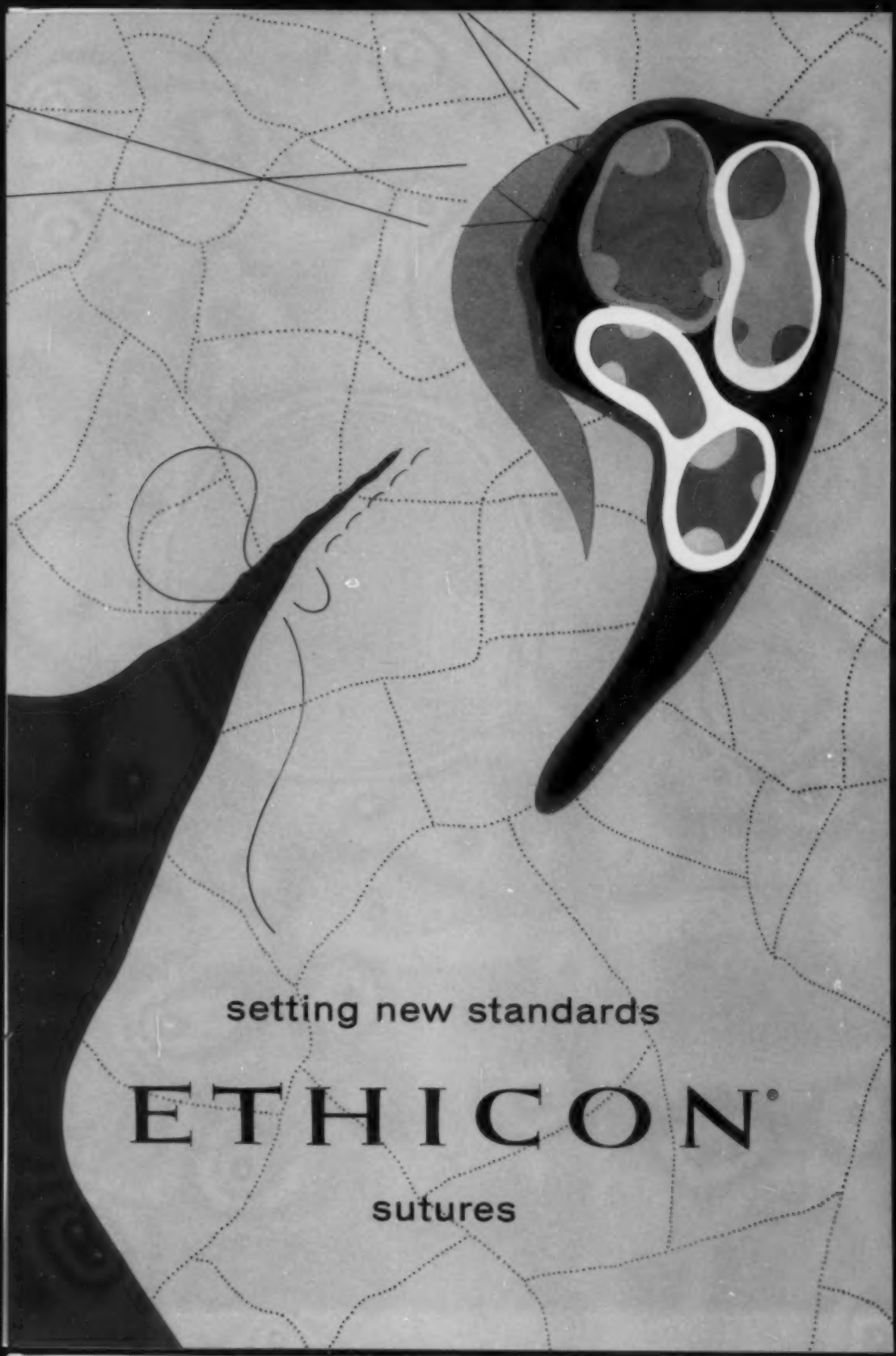
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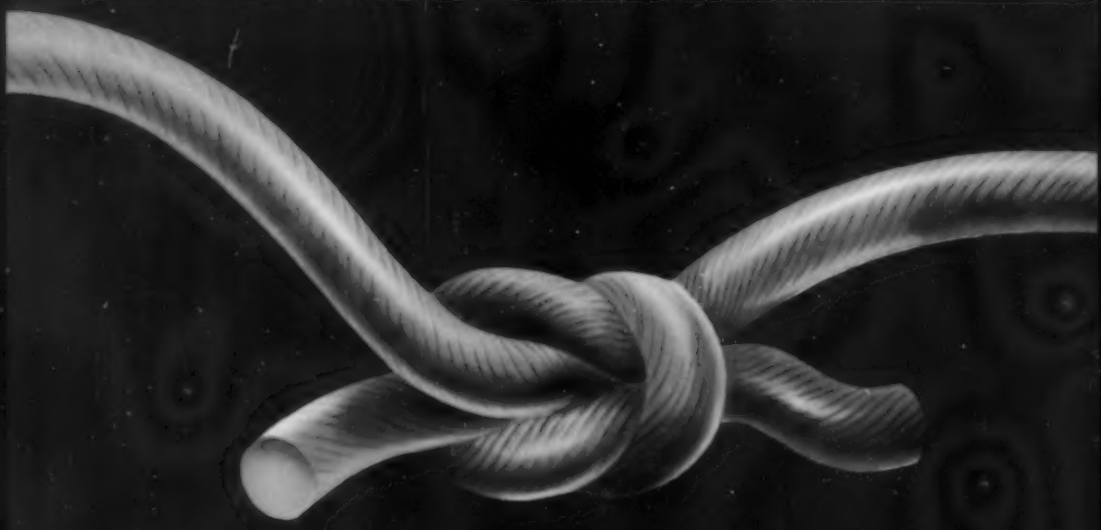

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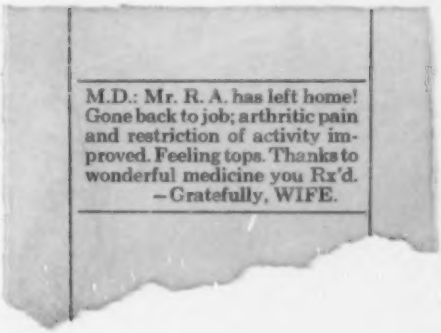
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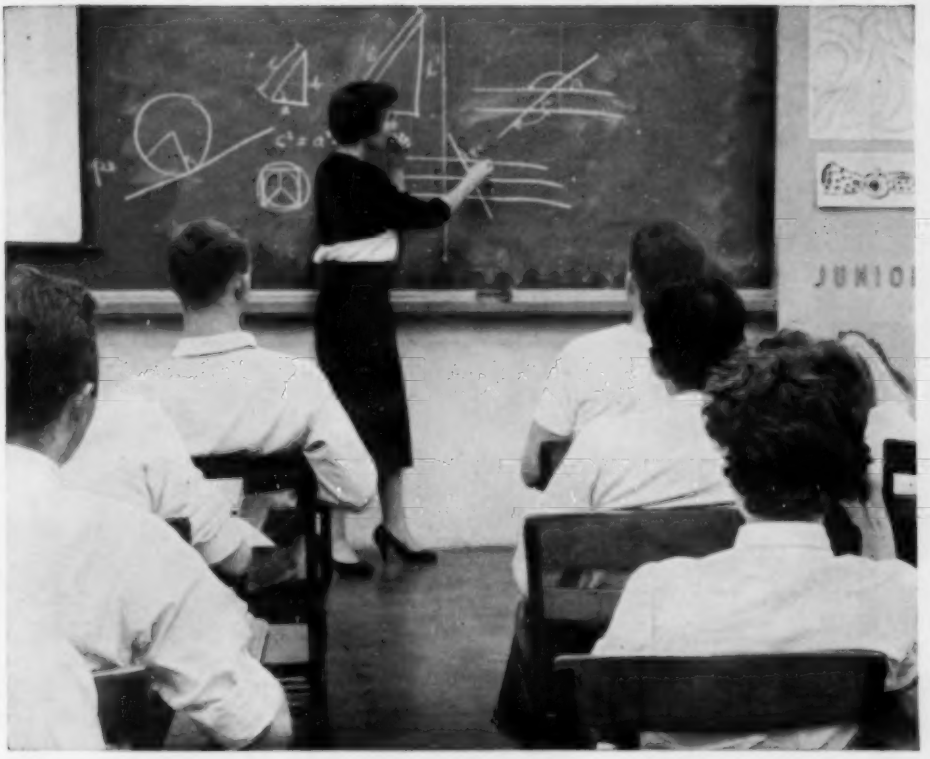

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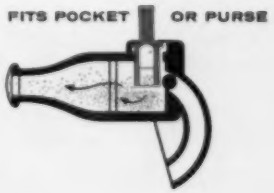

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*Chernish, S. M., and Pock, F. B., Jr.: Antibiotic Med., *1*:377, 1965.

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DISEASES of the CHEST

VOLUME XXXI MARCH, 1957 NUMBER 3

Symposium on Coronary Artery Disease
Blood Supply to Ischaemic Myocardium Distal to the Occlusion of a Coronary Artery

CLAUDE S. BECK, M.D., F.C.C.P.*

Cleveland, Ohio

A Self-Evident Truth[1, 2, 3, 4]

When a coronary artery is narrowed or occluded the fate of the human patient, or the fate of the experimental dog, depends upons the amount of blood in the ischaemic myocardium. This applies whether the stenosis or occlusion is produced by disease in a coronary artery or by surgical ligature of a coronary artery. The factual nature of this statement is comparable to the axiom in geometry that a straight line is the shortest distance between two points. Understanding and acceptance of this statement is the first requirement to understanding the coronary problem. It is also a requirement for the development of effective methods of treatment.

If these statements are correct, and no scientist can deny them, then an informed society will expect the medical scientist to investigate blood-supply to ischaemic muscle and to develop methods to increase it. A voluminous medical literature, which scarcely mentions this subject, does not have the answer to the coronary artery problem nor do the appeals for funds for research give any promise for effective treatment of coronary artery disease unless the research is directed to a study of blood-supply to muscle made ischaemic by the disease. My associates and I have investigated this problem over the past 25 years. This investigation was carried out in over 5,000 dogs; surgeons and physiologists devoted from one to five years on this project full time; experiments were done directly upon the coronary blood vessels; observations were made and facts were established. These facts have been published in the medical literature but in general the medical cardiologists have reacted to them as if they do not exist. In most instances their resistance is based upon a lack of understanding. However, surgeons are doing the operation with good results and an informed public will expect the medical cardiologist to cooperate in the best interest of the patient.

*Professor of Cardiovascular Surgery, Western Reserve University and University Hospitals.

Presented at the 22nd Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 7-10, 1956.

This work was supported by grants from the U. S. Public Health Service and the Cleveland Area Heart Society.

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Concerning the Amount of Blood Distal to the Occlusion

The amount of blood distal to the stenosis or occlusion determines the responses that occur after a coronary artery is narrowed or occluded. These responses by the heart are of two kinds. One concerns the production of electric currents; the other concerns death of heart muscle. These responses are related in that each concerns oxygenated blood in ischaemic myocardium but in other respects they are independent biological processes. Intelligent recognition of each of these responses is essential to further investigation of the coronary problem.

Oxygen Differentials in Myocardium, Electric Instability of the Heart, Ventricular Fibrillation[3, 4]

When the heart of a dog is exposed in the experimental laboratory and when the dog is well oxygenated by mechanical respiration the heart is uniformly pink. When electrocardiograms are taken from the surface of the heart the pattern of the electrocardiogram is the same from the entire surface of the heart. When the intratracheal tube is clamped off for periods of six to nine minutes the heart becomes markedly cyanosed. The pattern of the electrocardiogram from the cyanosed heart is identical to that from the well oxygenated heart. The uniformly pink heart and the uniformly blue heart are electrically stable. When the cyanosed heart stops beating it stops in asystole or standstill. It does not fibrillate. When a coronary artery is ligated in a well oxygenated heart an island of blue muscle appears in contrast to and in contact with pink muscle. The electrocardiogram now changes. The S-T segment is elevated over the blue and depressed over the pink muscle. The term oxygen-differential is applied to this change in oxygen content. This oxygen differential gives rise to electric currents at the precise plane of contact between blue and pink myocardium and these currents may be strong enough to fibrillate the heart. This heart has become electrically unstable. When the cyanosed heart is used and a coronary artery is cannulated and perfused with well oxygenated blood a pink island is produced in contrast to and in contact with blue muscle. The electrocardiogram again changes. The S-T segment is elevated over the blue and depressed over the pink muscle as in the other experiment. Again electric currents are produced and these may be strong enough to fibrillate the heart. This heart has become electrically unstable.

History and Significance of Oxygen Differentials

After having worked many years in the experimental laboratory to develop methods for delivery of red blood to the myocardium it was nothing less than a paradox that well oxygenated blood when delivered to the heart could destroy the heart beat. It seemed as though this should not be so. Our belief was that red blood should only help the heart. There was something wrong; science was withholding a hidden secret. And as long as it was hidden, we in the laboratory had a sense of confusion and frustration. From experience we knew that a cyanosed heart did not fibrillate, and that it stopped in standstill. To demonstrate cardiac standstill or asystole in our course in "Cardiac Resuscitation" we produced anoxia in over 60 dogs

and the heart always stopped in asystole. Almost by accident we took electrocardiograms from the surface of the cyanosed heart and found that the configuration had not changed while the heart was receiving no oxygen from the lungs. Then the hidden fact was recognized. It is not the amount of oxygenated blood to the heart that fibrillates it; it is differences in oxygen content in the muscle that fibrillates it. A heavy burden was lifted from our thoughts. Since 1932 we made triggers in the heart by producing anoxia. This was localized anoxia but at that time the localized nature of the anoxia had no special significance to us. We learned much from this concept of trigger. Now we had a reverse trigger. It did not take long to compare these two types of trigger and to measure the current in millivolts as the electrode was swept over the plane of contact between pink and blue and blue and pink on the surface of the heart. We knew that the term "current of injury" used by the physiologists was not applicable to this phenomenon and we coined the term "oxygen differentials" to designate it. We also began to use the terms electrically stable heart and electrically unstable heart and these terms have important significance.

The application of this discovery is far-reaching. It lays the foundation for the scientific approach to the coronary artery problem and a more effective form of treatment. The following questions and answers illustrate its application.

1. Does the amount of oxygenated blood delivered to the heart determine the electrical stability of that heart? Answer: no. In general a cyanosed patient has a stable heart. The heart of a congenitally cyanosed patient is stable. As a rule when it stops beating it does not fibrillate; it stops in asystole.

2. What produces the fatal heart attack in the presence of coronary artery disease? Answer: Stenosis or occlusion of a coronary artery reduces the blood supply to the muscle supplied by this artery. A current due to oxygen differential is produced and this current becomes strong enough to fibrillate the heart.

3. Can a current from the outside fibrillate the heart? Answer: yes. This occurs when a man is killed by lightning or when he is electrocuted. In the laboratory it is a simple matter to touch the heart with a wire carrying a faradic current and produce fibrillation.

4. In the presence of coronary artery disease how can oxygen differentials be reduced or prevented? Answer: This can be accomplished by the delivery of additional blood to ischaemic muscle by way of communications between one coronary artery and another.

5. How can this be accomplished? Answer: Surgical operation is the most effective method.

6. Is surgical operation effective by producing an even distribution of the blood that enters through the diseased coronary arteries or does it add additional blood to the heart from outside sources such as from tissue grafted upon the heart? Answer: Primarily the benefit is by the production of an even distribution.

7. Can an even distribution be produced by drugs? Answer: There are

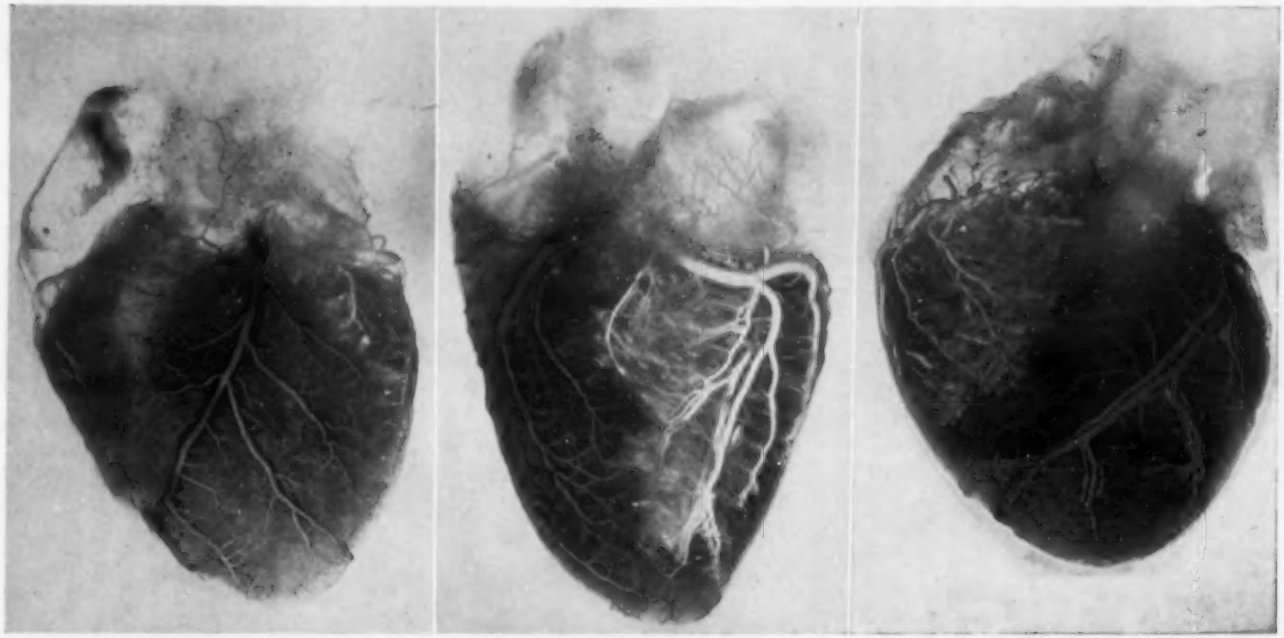

FIGURE 1A FIGURE 1B FIGURE 1C

Figure 1: Normal dog hearts with descending coronary artery injected in red and the circumflex and right coronary arteries injected in white. This material is thick and does not penetrate capillaries.—*Figure 1A* shows the anterior view of a heart—*Figure 1B* shows the area between descending artery and circumflex artery.—*Figure 1C* shows the area between descending artery and right artery. The communications between these arteries in the normal heart are sparse. The same holds true for the human heart. Only nine per cent of normal hearts show intercoronary arterial communications.

no scientific measurements to indicate that this occurs. There is short-term relief of pain by drugs but there is no evidence to indicate that they can improve the anatomy and physiology of the coronary circulation.

8. Is coronary artery occlusion an effective stimulus for the production of intercoronary communications? Answer: Yes, it is a very effective stimulus but it is not applicable as a method of treatment. Narrowing of an artery is effective only when it becomes occluded and many lives are lost while the narrowing becomes more and more marked until occlusion occurs. If the patient lives while the occlusive disease progresses to occlusion then excellent intercoronaries are produced.[6]

9. In the presence of coronary artery disease why operate when the occlusive disease is a "very effective stimulus" for the production of intercoronaries? Answer: Many people die as the narrowing process becomes more and more severe. During this process of narrowing, the intercoronaries are often not adequate to keep the currents below the fibrillation threshold.

10. If the patient survives occlusion is his heart protected? Answer: Yes, it is protected. A piece of muscle may be lost by the occlusion but intercoronaries are now present.

11. Is the heart adequately protected if it survives occlusion? Answer: Yes, provided the occlusive process remains static and does not spread to other coronary arteries. Some patients are as well as if they never had an occlusion.

12. What is the condition for those who get a second occlusion? Answer: The axiom for the disease holds true. The outcome depends upon the amount of blood beyond the second occlusion.

13. Can surgical operation augment the amount of blood beyond the occlusion of a second coronary artery? Answer: Yes, the first occlusion and the surgical operation both contribute to this protection.

14. Is it possible for a patient to be improved by operation so that he can return to his full time job, then after a period of months the symptoms recur and he becomes incapacitated again and dies from his disease? Answer: Yes, this has occurred. Coronary stenosis and occlusion may be progressive, and if progressive, operation cannot retard the occlusive process. The patient is improved by operation; later on the disease may progress and kill.

15. Can the result in this patient be classified as good or excellent? Answer: Yes, operation does not presume to cure the disease.

16. Can the medical cardiologist reasonably object to this point of view? Answer: If he objects he does not understand the coronary problem or the limitations of surgical operation.

17. Why do so many men fall over dead while shoveling snow? Answer: They die from electric currents. The stenosis may be mild; indeed the pathologist may not find it. The exercise quickens the circulation. The hands and face become pink; the heart becomes pink. The heart is well oxygenated everywhere except for an area of muscle supplied by a stenosed or occluded artery. Oxygen differentials are produced. The cold air inhaled

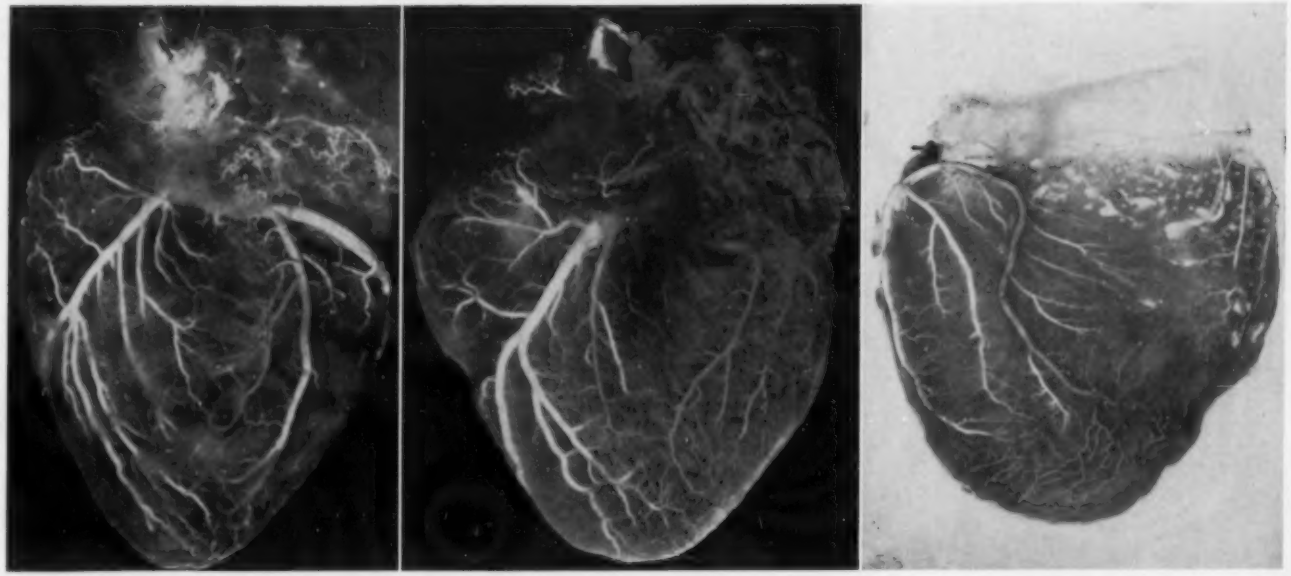

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2: Dog hearts after operation.—*Figure 2A* shows the area between the descending and circumflex arteries. Both arteries are injected in white.—*Figure 2B* shows the same view, except the circumflex artery was injected in red.—*Figure 2C* shows the posterior view. The descending artery was injected in red and the circumflex and right in white. The descending cannot be seen, but its branches communicated freely with the circumflex artery over the apex. An injection mass enters the circumflex artery from the descending. Intercoronary communications are seen in each of these specimens.

by the man cools the blood as it goes through the lungs and this in turn cools the heart. This hypothermia of the heart reduces the theshold of fibrillation and a small ineffective current in a warm room now becomes effective for fibrillation.[7] Had the man remained indoors the probability is that he would not have died.

18. Can oxygen delivered to a patient with coronary disease (oxygen tent) be detrimental? Answer: Consideration should be given to this question. I have no answer.

19. Can the death-factor in a fatal heart attack be reversed? Answer: Yes, this has been done.[8] It is often a small factor like stopping or starting the pendulum of a clock, like turning on or off the ignition switch in a motor car. It is reversible and also preventable.

20. Is it reversible when a man dies outside a hospital as on the golf course? Answer: Probably yes, if necessary equipment and personnel trained in resuscitation methods are immediately available. The anatomy of the heart in these victims is that of a good heart capable of continued function.

21. In what other way can coronary artery disease kill except by the production of electric currents? Answer: The heart may remain stable as the occlusive disease involves one artery after another. At no time are

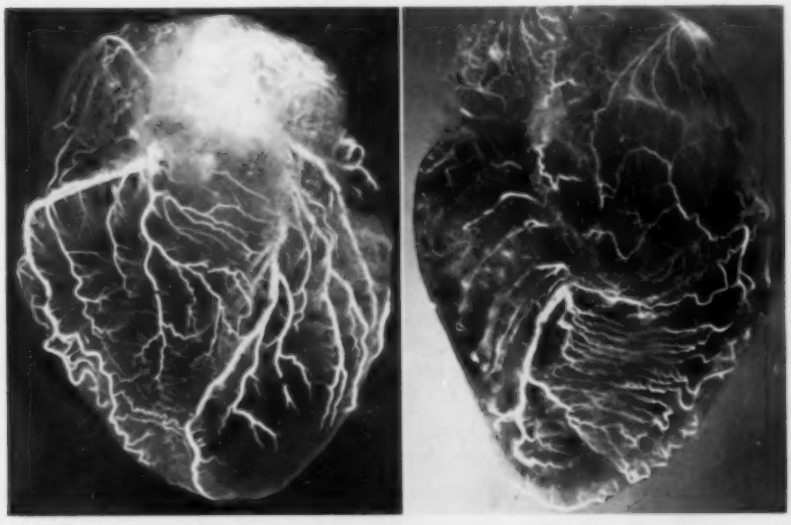

FIGURE 3A FIGURE 3B

Figure 3. Human heart. This patient had severe coronary artery disease and was operated upon. He was rehabilitated so that he could return to work without pain for nine months. Pain then recurred and he died after another three months. The arteries are injected in white. The descending artery is completely obliterated at its origin. The circumflex artery also shows disease. *Figure 3A* shows the anterior view and *Figure 3B* shows the posterior view. Three branches from the right are occluded and it is probable that this area produced pain, electric currents, and death. Note the intercoronaries over the auricles as well as over the ventricles. The result in this patient was classified as good or excellent. Operation does not presume to cure coronary artery disease.

the currents strong enough to fibrillate the heart. There is good distribution of the blood that enters the diseased arteries. However, a degree of ischaemia is reached when the heart muscle can no longer function and the patient dies in failure. Little or nothing can be done for these patients by surgical operation.

22. Does operation replace one type of death for another? Answer: Probably yes. It delays death by preventing early death from the electric currents.

23. Should operation be done early as a protection when the anatomy of the heart is good? Answer: Yes.

24. Should it be done as a prophylaxis in members of "coronary families"? Answer: My answer is yes. The operation would be done when the risk is zero and the heart would be protected if and when occlusion developed.

Surgical Operation[1, 2]

The crippled coronary artery circulation can be improved in various ways. The possibilities are: 1, direct approach to the arteries themselves; 2, to add blood from sources outside the heart; 3, to produce an even distribution of the blood that enters the diseased coronary arteries. These possibilities are not discussed here except to say that method three is the only effective method that can and should be applied to human patients. No

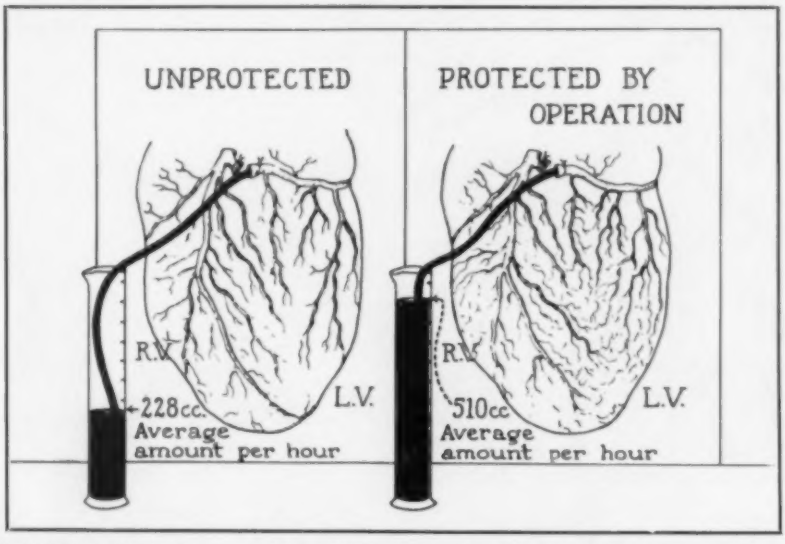

FIGURE 4: Mautz-Gregg backflows.[3] The circumflex artery is ligated at its origin and cut distal to the ligature. A catheter is inserted into the distal end and the amount of blood obtained is the back-flow. It is an indication of the amount available to the ischaemic myocardium beyond the occlusion. The sketch on the left indicates the average amount per hour obtained in 67 normal dog hearts. The sketch on the right indicates the average amount per hour obtained in 41 dogs' hearts after the operation had been done some time previously. Operation added 282 cc. per hour to the amount normally present. This is comparable to a transfusion of red blood into this ischaemic area and this additional blood is available at the crisis of arterial occlusion.

doubt development of the other two methods will take place in the future but many years of study in our laboratory have had a small yield of accomplishment. The operation to produce intercoronaries consists of four steps: 1, abrasion of the lining of the parietal pericardium and the surface of the heart; 2, narrowing of the coronary sinus; 3, application of an inflammatory agent to the surface of the heart; 4, application of mediastinal fat to the surface of the heart as a graft. Changes in the circulation produced by the operation are illustrated in Figures 1, 2, 3, 4.[9]

Limitations of Operation and Results

These must be reiterated so that the positive effects of operation can be understood and accepted. No treatment, medical or surgical, can restore degenerated muscle. No treatment can stop or retard the occlusive disease in the coronary arteries. No treatment can prevent an occlusion (with the exception of anticoagulants). No treatment can cure the disease, operation reduces anginal pain and many patients are completely relieved of pain. Many patients are rehabilitated so they can work. Many patients are relieved of precordial compression as early as one day after operation. Almost all the patients show some improvement after operation. It is almost necessary to see some of these patients to appreciate the results. Whether it delays death will be answered in the future by statistical study. Experimentally where all factors were scientifically controlled, it was proved that operation saved life. The relief of pain and the ability to return to work are adequate reasons for operation. The risk of operation is slight. In the last consecutive 74 patients operated upon the mortality was 0.

SUMMARY AND CONCLUSIONS

1. Treatment of coronary artery disease has limitations. Prevention of this disease would make treatment unnecessary but prevention is not now possible. The most effective treatment is that which delivers blood to ischaemic myocardium.

2. Surgical operation is the only method that can accomplish this and should be applied to patients.

3. The relief of pain is definite and often marked. Operation improves the coronary artery circulation, and by well controlled experimentation reduces mortality from artery occlusion. In the human it probably delays death.

4. The risk of operation is slight.*

RESUMEN Y CONCLUSIONES

1. El tratamiento de la enfermedad arterial coronaria tiene sus limitaciones. La prevención de esta enfermedad haría el tratamiento de esta enfermedad innecesario pero ahora esa prevención no es posible. El tratamiento más efectivo es el que prevea de sangre al miocardio isquémico.

2. La intervención quirúrgica constituye el método único que puede realizar esto y debe ser aplicado a los enfermos.

*One hundred consecutive patient were operated upon. The operative mortality was 0; one patient died from another occlusion before he was discharged from the hospital. There were no other deaths.

3. El alivio del dolor es definido y a menudo marcado. La operación mejora la circulación coronaria y de acuerdo con la experimentación bien controlada, reduce la mortalidad debida a oclusión coronaria. En el sér humano probablemente retarda la muerte.

4. El riesto de la operación, es pequeño.

RESUME

1. Le traitement des atteintes coronariennes est limité. Seule la prophylaxie de cette affection, qui n'est pas encore actuellement réalisable, rendrait le traitement inutile. L'action thérapeutique la plus efficace consiste à amener du sang au myocarde ischémique.

2. On ne peut parvenir à ce but que par une intervention chirurgicale et on devrait y faire appel pour les malades.

3. Le soulagement de la douleur est certain et souvent important. L'intervention améliore la circulation coronarienne artérielle. Une expérimentation bien contrôlée a montré qu'elle réduit la mortalité de l'oblitération artérielle. Chez l'homme elle augmente probablement la survie.

4. Le risque opératoire est minime.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

1. Die Behandlung von Koronararterienerkrankungen hat ihre Grenzen. Eine Verhütung dieser Erkrankung würde eine Behandlung überflüssig machen, aber eine Verhütung ist noch nicht möglich. Die best wirksame Behandlung ist diejenige, die dem ischämischen Myocard Blut zuführt.

2. Chirurgisches Vorgehen ist die einzige Methode, die dies zustande bringt, und sie sollte bei den Kranken Anwendung finden.

3. Die Behebung des Schmerzes ist endgültig und oft ausgesprochen. Die Operation verbessert die Zirkulation der Koronararterien, und aufgrund gut kontrollierter Experimente wird die Mortalität nach Arterienverschluss verringert. Beim Menschen hält sie wahrscheinlich den Tod auf.

4. Das Operationsrisiko ist gering.

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Surgical Treatment of Coronary Artery Disease: Medical Management and Evaluation of Results*

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Surgical operation has proved to be safe and effective in providing the patient with coronary artery disease a more adequate distribution of coronary inflow to the myocardium. That operation can be carried out safely is attested to by the fact that in the last 100 consecutive patients operated to date by Dr. Claude Beck in Cleveland, mortality associated with operation has been *zero*. Long-term follow-up has already demonstrated increased longevity in operated patients. Furthermore, nine out of 10 patients evaluated six months to five years after operation have little or no pain and are economically productive.

This section of the symposium is based upon clinical observations on approximately 500 patients evaluated as candidates for the surgical treatment of coronary artery disease since January, 1951. To date, the Beck I operation has been performed on 225. Approximately 150 have been rejected for operation because of certain contraindications, usually extensive muscle damage and myocardial failure. Another 12 patients were considered acceptable for operation but died of their disease while awaiting hospitalization. One died suddenly 12 hours preoperatively. Approximately 110 others were considered acceptable for operation but have refused for various reasons or have delayed hospitalization; this latter group will eventually serve in a control series.

The clinical results associated with operation merely confirm the extensive laboratory evidence of benefit.[1] Ideally, operation is an elective procedure to be applied as early as possible in the clinical course of coronary artery disease. Unfortunately, for many years surgical treatment was applied only to salvage patients in whom little could be achieved. Probably the greatest single deterrent to elective application of surgery has been the fear of high mortality expected of any surgical procedure performed on patients with severe coronary disease (however, with little consideration for the prohibitive mortality associated with standard medical therapy).

The demonstration of protection afforded by operation, with a remarkably low operative mortality, presents a challenge to the cardiologist. Unless definitive medical therapy can significantly modify the mounting disability and mortality resulting from coronary disease, the patient with this disease should be considered as a candidate for operation. Furthermore, skillful medical selection and supervision of patients in close cooperation with the surgeon is the *sine qua non* in achieving the excellent results that can be demonstrated.

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Early in the development of the operation for coronary disease it was presumed that selection and evaluation of patients could be carried out best by a committee of cardiologists, each performing his own evaluation. Unfortunately, particularly in caring for the anxious patient with coronary disease, such a cold, "objective" approach tends only to increase his anxiety and rob him of the vital doctor-patient relationship. Ideally, a single competent cardiologist can offer both reassurance and careful evaluation.

Indications for Operation and Classification of Patients:

The one indication for operation is a positive diagnosis of coronary disease. The achievement of a low operative mortality now justifies the application of the operation to patients with "early" disease, before extensive myocardial damage has occurred. By the same token, the protection afforded by operation need not be withheld until the patient has had at least one myocardial infarction; early operation can reduce the 10- 20 per cent mortality associated with the first episode of myocardial infarction. Operation may also be performed even after several episodes of infarction, but obviously little benefit can be achieved if the heart has begun to dilate.

Classification of patients with coronary artery disease is particularly difficult. Consideration must be given not only to the degree of myocardial degeneration but also to the progression of the occlusive process in the arteries. The following preoperative classification has been found useful:

Group 1. Patients with mild symptoms. Usually under 50 years of age. May have small infarct and/or mild angina.

Group 2. Moderately advanced disease. Moderate to severe angina. May have one or more infarcts. Normal heart size.

Group 3. (a) Salvage cases. Extensive muscle damage. May have large heart and congestive heart failure.

(b) Status anginosus.

(c) Certain contraindications.

The great majority of patients operated on are in Group 2. However, fortunately, the percentage in Group 1 is increasing. As a matter of fact, in members of families with a "bad" coronary history, operation should be considered at the earliest evidence of the disease.

Contraindications:

Acute myocardial infarction, or even suspicion of impending infarction, precludes operation for at least four to six months. In addition to the obvious dangers of operation during the acute stage, the delay allows for development of natural compensatory mechanisms. Operation is also hazardous in younger patients with rapidly progressive symptoms, particularly in those without previous myocardial infarction. These patients are prone to the development of areas of ischemia during or immediately after operation. These hearts tend to develop electrical instability[2] with resultant ventricular fibrillation, so that an impending medical death becomes a surgical mortality.

Cardiac enlargement and evidence of congestive failure constitute a

relative contraindication to operation. However, in 20 per cent of the patients operated on in this series, the left ventricle was fluoroscopically enlarged. At least one-fourth of them had objective evidence of early congestive failure. Although it is too late for much benefit in such cases, the heart is remarkably stable and they tolerate operation quite well.

Severe hypertension, or any other associated disease which, *per se*, limits life expectancy, contraindicates operation. However, a moderate degree of blood pressure elevation was present in 25 per cent of those operated.

Age and Sex:

In this series of 225 patients operated, the age range was 27 to 72 with an average age of 48 years. Generally, those over the age of 65 carry an increased operative risk, but operation is not denied such a person if his tissue-age justifies it. Twenty in this series were over 60. In those under 40 years of age, the rapidly progressive disease usually present in this age group tends to make operation somewhat hazardous. However, operation was carried out in 30 under 40 years of age. Less than 10 per cent of the patients operated were women.

Symptoms and Duration:

In the present series, 75 per cent had suffered at least one clinically proved myocardial infarction. Two or more infarctions had occurred in 20 per cent. Angina pectoris, ranging in severity from mild to complete status anginosus, was present in 95 per cent of the patients operated.

The duration of symptoms, *per se*, of course gives no indication of the severity of the disease. The range in this series was four months to 13 years with an average of 2.9 years. In general, those with longer duration of symptoms appeared to tolerate operation better.

Preoperative Management:

The purpose of the preoperative study is to establish the diagnosis and to rule out contraindications to surgery. In persons with coronary artery disease, extensive diagnostic procedures do *not* constitute good medical management and actually may be dangerous. This fact was painfully demonstrated in the following two cases: Early in this series, in one with classical angina and an old posterior myocardial infarct, a gall bladder series was ordered "to rule out any other possible causes of chest pain." Soon after he ingested a large number of tablets for visualization of the gall bladder, he developed nausea and severe vomiting, followed by sudden death. In another, severe pain with evidence of an acute anterior myocardial infarction occurred suddenly as he was complaining bitterly during a barium enema. Death occurred 24 hours later. In both cases it is presumed that death was at least precipitated by unnecessary traumatic procedures.

Such usually superfluous procedures as the electrocardiographic exercise tolerance and anoxemia tests should be performed only when the diagnosis is in doubt. In a patient with a critically compensated coronary circulation, undue stress may produce catastrophic consequences. Obviously, in one

with electrocardiographic evidence of old infarction such tests are contraindicated. Furthermore, in one with typical symptoms, a negative test in no way alters the diagnosis.

The preoperative hospital stay should be as short as possible, usually less than five days. Exhausting tests are particularly contraindicated on the day before operation. Anxiety and apprehension appear to have a specific deleterious effect, and such patients have a greater operative risk, presumably associated with the lowered fibrillation threshold of the heart.[2] Operation should be delayed until anxiety is allayed or at least reduced.

Reduction of Thyroid Activity:

In five in this series hypothyroidism had been previously induced by medical or surgical means. They had been seriously incapacitated and had not been significantly benefited by this treatment. Operation was considered particularly dangerous in such cases. However, they tolerated operation remarkably well; their hearts showed greater stability than euthyroid patients. Thyroid-epinephrine relationships are such[3] that reduction in thyroid activity appears to play an important role in raising the fibrillation threshold of the heart. In accordance with these observations, in those with rapidly progressive disease (status anginosus) or severe anxiety, who are prohibitive risks for surgery, pre-treatment with anti-thyroid drugs appears to decrease significantly the operative risk.

Once it has been determined that there are no contraindications to operation, the procedure is carried out as soon as possible. Under no circumstance is operation performed unless the patient and spouse are in complete agreement and reasonably receptive. Furthermore, they must understand not only what operation can do, but also what it cannot do.

Preoperative Digitalization:

Prior to surgery all patients are completely digitalized. This is done even though there is no evidence of congestive failure. Contrary to certain theoretical concepts, digitalis definitely *decreases* myocardial irritability during operation. The various ventricular and supraventricular arrhythmias associated with cardiac surgery are significantly diminished by adequate digitalization. Specific beneficial inotropic and chronotropic effects are evident. In inadequately digitalized patients, annoying sinus tachycardias can be controlled by supplementary intravenous digitalis administration. The routine use of digitalis has been an important factor in achieving a remarkably low operative mortality.

At first, digitalis was used only sporadically and against the better judgment of most cardiologists. However, it soon became obvious that digitalis did not have the expected deleterious effect but seemed to maintain greater stability during operation. This observation was further strengthened during resuscitation experiments in the dog laboratory. Digitalized dogs could be resuscitated more readily and more frequently than those non-digitalized, and had a greater resistance to reversion to ventricular fibrillation.

Digitalization is continued until discharge from the hospital. However,

in those with cardiac enlargement and extensive damage, maintenance digitalis is recommended.

Management During Operation:

During operation, the surgeon, anesthesiologist, and cardiologist must observe close teamwork. Although the surgeon assumes the major responsibility, the cardiologist must be in command. Continuous electrocardiographic monitoring is essential. Various pharmacological agents and rest periods are judiciously applied as indicated. In most cases, however, operation proceeds from beginning to end without interruption. Of course it is desirable that operation be carried out as expeditiously as possible. However, there need never be undue haste. The duration of operation, within certain obvious limits, is in no way a consideration in the successful outcome. With good anesthetic management, oxygenation and maintenance of circulation during operation should be as adequate as that prior to induction of anesthesia.

A mechanical respirator (Rand-Wolfe) is always used. In refutation of theoretical objections to such a respirator, one need only point out the remarkably benign course of these patients. Oximetry and direct arterial saturation studies during operation have demonstrated the maintenance of a constant high level of arterial saturation throughout operation. Probably more important than the absolute level of arterial O_2 saturation, is the necessity for avoiding marked variations in oxygenation (such as have been demonstrated by oximetric studies during irregular intermittent manual compression of the bag). Sudden variations in myocardial oxygenation may produce dangerous oxygen differentials in the myocardium leading to ventricular fibrillation.[2]

During cardiac manipulation various ectopic beats occur. Especially during epicardial abrasion, frequent ventricular premature beats and even runs of ventricular tachycardia appear, but subside immediately when abrasion ceases (Figure 1). Only rarely do these ectopic beats persist. There has been no instance of persistent ventricular tachycardia or fibrillation associated with this manipulation. So-called anti-fibrillatory drugs should not be used routinely. Procaine amide or quinidine should not be used empirically, in view of the myocardial depression produced. Only rarely is it necessary to use even small amounts of procaine amide for a particularly irritable heart.

The epicardial abrasion is frequently associated with ST segment deviations (Figure 2). Although there may be ST segment depression in the left arm lead and reciprocal ST elevation in the foot lead, these deviations are transient and return to the isoelectric line within a few days of operation. Rarely ST segment deviations followed by QRS changes suggestive of acute infarction appear soon after operation. Evaluation of such electrocardiographic findings is, of course, difficult. Serum transaminase levels[4] have been of value in estimating the degree of myocardial necrosis associated with operation and in diagnosing myocardial infarction following operation.[5] At the end of operation, all patients show a significant rise in serum transaminase. The peak is reached 48 hours postoperatively

and generally is within normal limits by the fifth day. A sudden rise or undue elevation is indicative of acute myocardial infarction.

During operation, especially soon after induction of anesthesia, moderate bradycardia and hypotension may occur. Small doses of atropine sulfate (0.2 milligrams intravenously) specifically prevent a potentially dangerous slowing of the heart. Whenever moderate hypotension occurs, a rest period is observed and the lungs are well inflated. A small dose of atropine may then be tried. If hypotension persists, a gentle vasopressor (mephentermine, seven and a half to 15 milligrams intravenously) is given. Frequently this produces a sustained rise in pressure, although occasionally repeated doses are required. Rarely a more potent vasopressor drug (nor-epinephrine) is required. Generally, there is remarkably little fluctuation of blood pressure during the operation.

Examination of the heart at operation affords an excellent method for correlation with clinical impressions. The major coronary vessels are inspected and palpated with reference to tortuosity, pulsations, and patency. The heart size and character of pulsations are evaluated. Areas of scarring can be mapped out. By means of direct epicardial electrodes, accurate electrocardiographic survey of the myocardium has been carried out in many patients.

Operative Mortality:

Of the 225 patients operated since January, 1951, there have been 11 deaths associated with surgery (two during operation, nine in the early postoperative period), for a total mortality of less than five per cent. Care-

FIG. 1

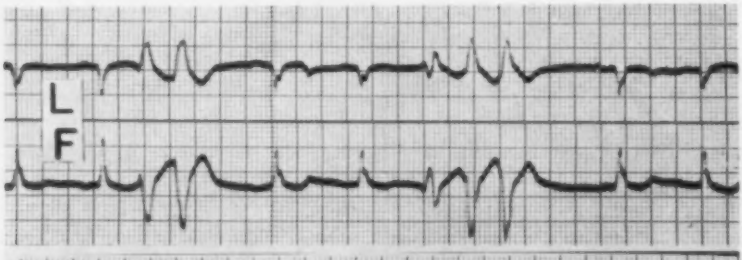

FIG. 2

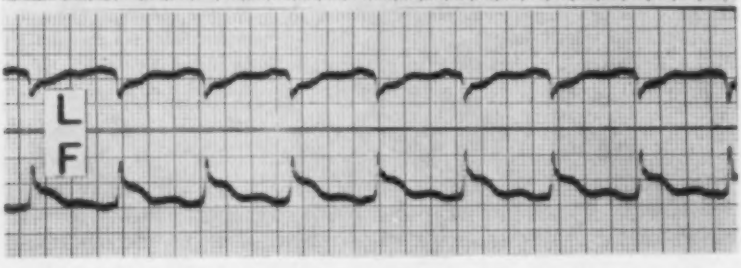

Figure 1: Electrocardiographic observations during operation. Simultaneous unipolar left arm (L) and foot (F) leads show frequent ventricular premature beats associated with epicardial abrasion.—*Figure 2:* Electrocardiographic observations during operation. ST segment depression in left arm (L) with reciprocal elevation in foot lead (F) following abrasion of diaphragmatic surface of heart.

ful selection of patients and improvements in medical and surgical management have resulted in a progressive lowering of operative mortality, as evidenced by a series of 100 consecutive operations without a death. At least 30 of these 100 patients were salvage cases. However, in every instance symptoms had become fairly stable for a few months prior to operation. Recognition of the limitations of operation has prompted judicious delay in those seriously ill. Certainly, if a catastrophe is imminent, an ill-timed operation will only hasten it. A delay of a few months permits time for stabilization and greatly enhances toleration of operation and the achievement of a good result.

Course of Patients After Operation:

The immediate postoperative course is remarkably uneventful, even in those who appeared severely ill before. Rarely does the patient complain of pericarditis pain (even though the postoperative electrocardiogram most frequently shows such a configuration). Small left pleural effusion is frequent, but only rarely requires thoracentesis. Evidence of pericardial effusion is rare. In no case has long-term follow-up revealed evidence of deleter-

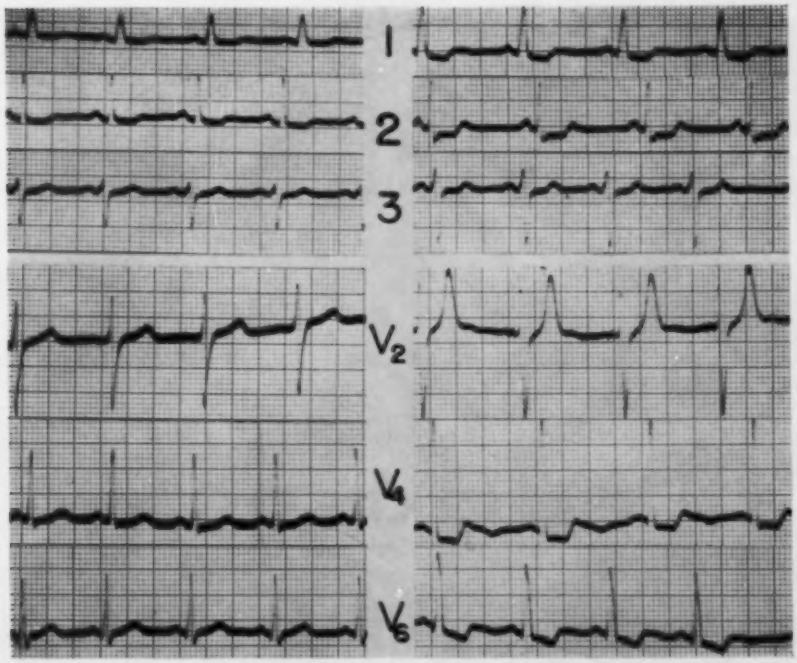

FIGURE 3: Exercise tolerance test in a patient with severe angina prior to operation. The three standard limb leads and three chest leads show a normal control record (on the left). After only 15 ascents the patient had severe pain and developed marked electrocardiographic evidence of myocardial ischemia; ST-T deviations are present in all leads after exercise (on the right).

ious effect of the operation itself. Compression of the heart by a pericardial scar has not occurred.

In approximately 25 per cent there is almost immediate improvement in symptoms, so that a few days following operation they volunteer the observation that a given amount of exertion no longer causes pain. Generally, following discharge eight to 12 days after operation, they are encouraged to return to at least part-time work in four to eight weeks.

In the great majority there is progressive improvement over a course of one to six months after operation. Occasionally, one may show no improvement for a few months followed by a period of rapid and dramatic subsidence of symptoms.

Long-term follow-up of the first 100 alive at this time reveals a significant observation: At least 15 of them have had one or more severe "attacks" requiring hospitalization. However, in only three instances was there definite evidence of transmural myocardial infarction. Each one recovered and eventually returned to work with no worsening of symptoms. The other 12 have had one or more bouts of severe precordial pain (one has had five) associated with transient T-wave changes in the electrocardio-

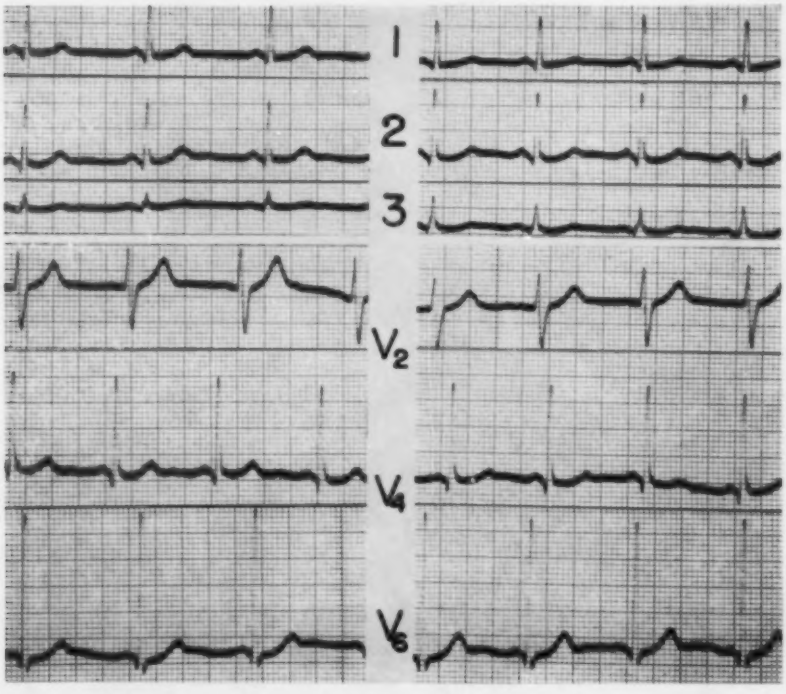

FIGURE 4: Improvement in exercise tolerance test following operation. (Same patient as in Figure 3.) Nine months after operation the control record (on the left) is still normal. After 25 ascents there is no significant change: A negative test. This was consistent with a marked reduction in the patient's angina.

gram. Usually, the pain subsided rapidly and they returned to work in one to four weeks.

In only 10 per cent did long-term follow-up reveal no improvement. However, in some of these there were such complications as severe narcotic addiction, psychoses, and cerebrovascular accident.

Remarkably enough, three who had evidence of early congestive heart failure prior to operation appeared to be much better compensated after operation. One of these, who had previously required weekly mercurial injections, has now gone eight months without injection.

Unfortunately, the very nature of coronary artery disease is such that so-called *objective* methods for evaluation of medical or surgical treatment are of little value. Reliance on the electrocardiogram or ballistocardiogram is unrealistic. Generally speaking, each one serves as his own control. No doubt, with a few more years of follow-up, a statistically significant evaluation will be forthcoming.

Evaluation of Objective Studies:

Serial electrocardiograms have been obtained in all patients before, during, and at regular intervals following surgery. Preoperative evidence of a myocardial infarct merely confirms the diagnosis. Postoperatively, invariably there are characteristic changes of pericarditis with eventual return to the preoperative pattern. Obviously, electrocardiographic evidence of myocardial regeneration is not to be expected. However, it is significant that in less than 20 per cent now living is there electrocardiographic evidence of further muscle destruction.

Early in this series, in an attempt to achieve a satisfactory objective method for evaluation, the standard exercise tolerance tests and the

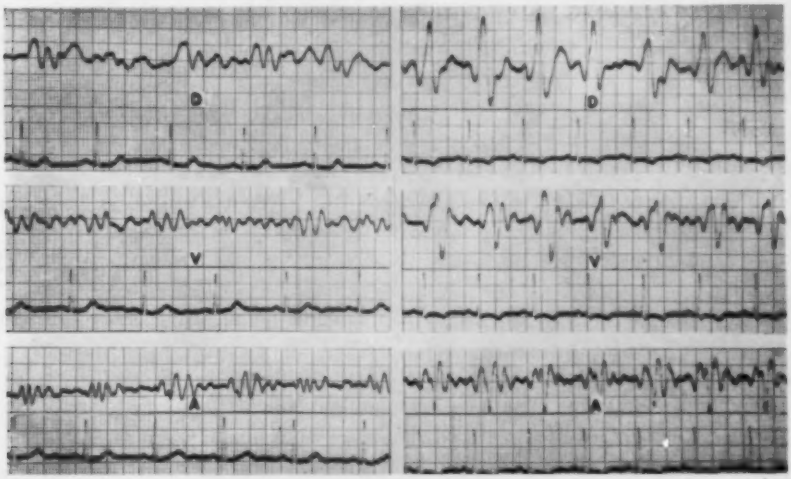

FIGURE 5: Ballistocardiographic improvement following operation. (D—displacement, V—velocity, A—acceleration.) The preoperative record (on the left) is grossly abnormal in a patient with moderate angina. One year after operation, obvious ballistocardiographic improvement is consistent with clinical improvement.

anoxemia tests were applied even in those with evidence of previous myocardial infarction. However, the lack of correlation between these tests and the degree of coronary disease was discouraging. Furthermore, since the operative procedure results in a permanent pericarditis, electrical repolarization is interfered with, so that ST segment changes following exercise are difficult to evaluate. In many patients there has been excellent correlation between changes in the exercise tolerance tests and clinical improvement (Figures 3 and 4). However, in at least two with negative exercise tests prior to operation, subsequent tests have been positive despite marked clinical improvement.

The displacement, velocity, and acceleration ballistocardiogram (Arbeit Apparatus) has been grossly abnormal in more than 75 per cent tested prior to surgery. Generally, in the first week after surgery, a characteristic deterioration is demonstrated. However, in approximately 15 per cent studied, evident improvement over the preoperative tracing occurs by the end of the second week. In at least 50 per cent of the long term studies, there has been eventual improvement in the ballistocardiographic tracings (Figure 5). However, there is no obligate correlation with the patient's status.

Longevity:

Long-term follow-up has been carried out on the 137 consecutive cases discharged over a period of six months to five years ago (average: two years since operation). The expected mortality in such a group over this period would be 30 per cent or 41 dead.[6] Actually 18 are known or assumed to be dead, a mortality of 13.1 per cent. Thus, even at this relatively early period, life expectancy can be shown to be increased by operation. Since operation does not prevent the occlusive process in the coronary arteries, a period of symptomatic improvement may be terminated by overwhelming occlusion and death. Such was the case in 50 per cent who died six months to five years after operation.

Present Status of Operated Patients:

Of the 100 consecutive patients who were alive and could be evaluated over a six month to five year follow-up period, 45 are completely free of heart pain. Another 45 claim that they have considerably less pain than before operation. Thus, 90 per cent have symptomatically excellent results.

By the same token, 42 are able to work with no limitations, while 48 are better able to work with some limitations. Thus 90 per cent are economically productive. (Prior to operation only 45 per cent had been able to work half-time or more).

SUMMARY AND CONCLUSIONS

The Beck operation for coronary artery disease is a safe and effective method for providing a more adequate distribution of arterial blood supply to the heart. Operation is indicated in patients with a positive diagnosis of coronary artery disease unless there is a specific contraindication. The operation should not be considered as merely a salvage procedure. Best results are obtained by operating early in the course of the disease.

In the last 100 patients operated, the mortality associated with operation has been zero. The over-all mortality for 225 operated since January, 1951 is less than five percent. Long-term follow-up reveals a significant increase in longevity for operated patients. Furthermore, 90 per cent were back at full time or part-time work with little or no limitations.

In view of the proved effectiveness of the Beck operation for coronary disease, the demonstration of a low operative mortality removes the operation from the category of salvage procedures and justifies its early application to a majority of persons with coronary disease.

RESUMEN Y CONCLUSIONES

La operación de Beck para la enfermedad coronaria es un método seguro y efectivo para proporcionar una mejor distribución sanguínea arterial al corazón. La operación está indicada en enfermos con el diagnóstico de enfermedad coronaria a menos que haya una contraindicación definida.

La operación no debe considerarse como intervención tan sólo de rescate. Los mejores resultados se obtienen operando tempranamente en el curso de la enfermedad.

En los últimos 100 enfermos operados la mortalidad dependiente de la operación, fué nula. La mortalidad global en 225 operados des de Enero de 1951 es menos de 5 por ciento. El seguimiento a largo plazo revela un aumento significativo en la sobrevida de los enfermos. Más aún, 90 por ciento regresaron a trabajar tiempo completo o parcial con pocas o ningunas limitaciones.

En vista de la efectividad demostrada de la operación de Beck para la enfermedad coronaria, la demostración de la baja mortalidad de la intervención la segrega de la categoría de procedimiento de último recurso y justifica la aplicación en la mayoría de las personas con afección coronaria.

RESUME

L'opération de Beck comme traitement de l'atteinte coronarienne est une méthode sûre et efficace, qui assure au coeur une distribution plus convenable de sang artériel. L'opération est indiquée quand on a porté nettement le diagnostic de maladie coronarienne, à moins qu'il n'y ait une contre-indication définie. L'opération ne devrait pas être considérée comme un simple sauvetage. Les meilleurs résultats sont obtenus en opérant dans un stade précoce de l'évolution de l'affection.

Chez les 100 derniers malades opérés, la mortalité opératoire a été nulle. La mortalité globale pour 225 opérés depuis janvier 1951 est moin de 5%. Des contrôles à longs intervalles de temps montrent une augmentation importante de la longévité pour les malades opérés. De plus, 90% ont repris leur travail à plein temps ou à temps partiel sans grande limitation de leur activité.

La démonstration de l'efficacité de l'opération de Beck dans la maladie coronarienne, la certitude d'une très faible mortalité opératoire, justifient que l'on ne classe pas cette intervention parmi les méthodes de simple

sauvetage, mais qu'on l'applique précocément à la plupart des individus souffrant de thrombose coronaire.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Die Beck'sche Operation bei Koronararterien-Erkrankung ist eine sichere und wirksame Methode zur Gewinnung einer besser angepassten Verteilung der arteriellen Blutzufuhr zum Herzen. Die Operation ist angezeigt bei Kranken mit einer tatsächlichen Diagnose einer Koronararterien-Erkrankung, sofern keine ausgesprochene Kontraindikation vorliegt. Die Operation darf nicht als eine blosse Rettungemassnahme angesehen werden. Die besten Resultate werden dann erzielt, wenn in einem frühen Krankheitsstadium operiert wird.

Bei den letzten 100 operierten Patienten betrug die Operations-Mortalität Null. Die Gesamt-Mortalitat bei 225 seit Januar 1951 operierten Kranken beträgt weniger den 5%. Sich über lange Zeit erstreckende Nachkontrollen ergaben eine beträchtliche Zunahme der Lebenserwartung für die operierten Patienten. Darüber hinaus hatten 90% ganz oder teilweise ihre Arbeit wieder aufgenommen mit geringen oder gar keinen Einschränkungen.

Im Hinblick auf die bewiesene Wirksamkeit der Beck'schen Operation bei Koronar-Erkrankungen hebt der Nachweis der geringen Operations-Sterblichkeit die Operation aus der Kategorie der Rettungsmassnahmen heraus und rechtfertigt ihren frühzeitigen Einsatz bei einer Mehrheit von Personen mit Koronar-Erkrankung.

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Anatomical and Physiological Considerations in the Development of a Collateral Circulation to the Myocardium

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1. *Introduction*

I wish to present our concept of collateral circulation in the heart as it is related to the problem of coronary artery disease in man. The physiological information has been largely derived from studies on the dog heart. We believe that the information derived from these physiological studies is directly transferable in building up a concept of the clinical problem in man, including the evaluation of methods of therapy. I wish to acknowledge that Dr. Claude S. Beck has been the originator of the surgical approach to the treatment of coronary disease and has been the chief proponent of the studies that have been carried out during the past 24 years.[1]

The development and application of precise physical methods of accurately recording and measuring fluctuating intravascular pressures by Frank, Wiggers and Hamilton has provided much basic information about normal cardiac function and hemodynamics. The further application of these principles and refinement of methods for the study of the coronary circulation by Gregg, Green and coworkers has provided accurate information about the coronary circulation in the normal heart.[2] The further application of these and similar methods of study must ultimately provide us with the complete knowledge of the changes that take place in the myocardial circulation when coronary arteries are progressively obstructed. Furthermore, the physiological information will then clearly explain anatomical findings and be integrated into a clear understanding of the total aspects of coronary disease. I wish to acknowledge that Drs. R. W. Eckstein and D. S. Leighninger have made especially significant physiological contributions in various phases of this problem.

2. *Historical*

It is self evident that no rational concept of collateral circulation could exist prior to the understanding of the circulation of blood as first reported in detail by William Harvey.[3]

Our basic knowledge about collateral circulation of the myocardium, which may be considered the emergency blood supply available when the normal blood supply is interrupted, involves anatomical, physiological and metabolic areas of study. As various isolated fragments of information became known about the anatomy of the vascular system of the heart and about the function of the myocardium, various hypotheses were formulated

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to indicate possible alternate channels of blood flow when the normal flow is interrupted. These hypotheses have led to a considerable conflict of ideas which are being resolved with the advent of reliable methods of measuring blood flow.

The earliest hypotheses of the mechanism of collateral circulation were the result of purely anatomical studies. The existence of anastomoses between coronary arteries was known in the 17th century[4] during which period the exploration of the finer ramifications of the vascular system by the injection of dyes was begun.

In 1706 and 1708 the publications of Vieussens and Thebesius[5, 6] described the channels connecting the coronary vessel directly with the chambers of the heart. The anatomical knowledge of these vessels later led to a long and fruitless controversy as to their functional significance, especially their possible role as avenues of collateral circulation. However, in the year 1880 Ludwig Langer,[7] in a report of his studies of the Thebesian channels in injected specimens of human hearts, made the following observation concerning the anastomoses of coronary arteries:

"I was able to demonstrate in several hearts injected with a fine resin mass several visible connecting branches between the right and left coronary arteries. These connecting branches ran transversely across the front surface of the heart and lay immediately under the epicardium. In these vessels the various colored masses which were injected into the coronary arteries met before a filling of the capillaries or veins took place." Langer continues: "The mentioned communications of coronary arteries with each other is not so unusual when one considers that the blood vessel system of the heart is not represented as an isolated whole. The vasa propria of the heart, as is known, anastomose much more with the vessels of the neighboring organs in a rich manner and indeed not only in the venous domain but also in the arterial territory. Such an anastomosis exists with the vessels of the pericardium as well as with the bronchial vessels and with the vessels of the diaphragm through the medium of the vasa vasorum of the large vesels emerging from the heart. By injection of the coronary arteries there is regular filling of the vasa vasorum of the cavae, the aorta, the pulmonary arteries and veins." Langer concludes: "The described anastomoses of the vasa propria of the heart with other vessels is noteworthy in clinical relationships. They provide the possibility that the heart can also be nourished with blood through collateral circulation when one or both branches of the coronary arteries are made impervious as a result of an atheromatous process—and it is well known that the atheromatous process is unusually frequent in the coronary arteries."

F. H. Pratt,[8] working in W. T. Porter's physiology laboratory published some interesting observations and ideas in 1898. "Many anatomists and physicians still contend in the face of conclusive experiments that the coronary arteries are not truly *terminal*. How else can such immunity from infarction be explained? What but a collateral circulation through branches freely communicating with other coronary arteries could have kept the ever active muscle from decay? The failure of the distal end of

a severed coronary artery to bleed in the profuse way that indicates a free communication with other vascular areas; the fact that infarcts frequently though not invariably follow the embolism or thrombosis of these vessels during life; and most conclusive of all the easy production of infarcts by ligation of coronary arteries, have not convinced some minds. They cling to the occasional freedom from infarction after thrombosis or embolism and not seldom attempt to strengthen their position by pointing to the fact that one coronary artery can be injected from another. These writers forget what a terminal artery really is. They forget that terminal arteries, like all other blood vessels, communicate with their neighbors by capillaries."

"An artery is terminal, not because it has no communications with neighboring arteries but because this communication is of a particular kind. *Terminal* simply implies that the resistance in the anastomosing branches is greater than the blood pressure in the arteries leading to these branches. It is this resistance which makes an artery terminal. This concept is physiological and only secondarily anatomical. Only injections that *pass with great ease* can be considered as presumptive evidence against the terminal nature of an artery; and as a fact aside from rare abnormal cases injections pass from one coronary artery to another with difficulty or not at all. The advocates of free anastomosis of coronary arteries have indeed a difficult position. They must explain how infarcts can follow closure of freely anastomosing vessels. We who believe in the terminal nature of these arteries need only to explain why the closure occasionally fails to produce infarction. An explanation of this can now be given." Pratt was referring to his demonstration that the cat myocardium will resume regular contractions and continue beating for a long time if either the right ventricular cavity or the coronary veins of the non-working cat heart are perfused with defibrinated oxygenated blood under low pressure. Under these circumstances it was presumed that the myocardium was nourished by retrograde flow through the capillaries via the Thebesian and coronary veins. Pratt stated further "It is also possible that a very gradual closure of an artery might permit the gradual dilatation of the communicating vessels until the resistance in them is low enough to divert a part of the blood in the neighboring areas into the anemic district; and thus gradually establish sufficient collateral circulation to keep the part alive. These possibilities have long been recognized."

In 1907 Hirsch and Spalteholz[9] experimentally ligated the descending ramus of the left coronary artery of dogs and monkeys, and on the basis of injection studies and the size of the resulting infarcts concluded that there was a functional collateral circulation from other coronary arteries. They were of the opinion that the anastomoses of the dog were comparable to those found in the human heart.

An observation of significance consisting of a single case report was recorded in the literature in 1903 when Ch. Thorel[10] described the heart of a man of 68 who died of carcinoma. At autopsy both coronary arteries were found to be obliterated in their proximal portions. The existence

of extensive pericardial adhesions was thought by him to have provided vascular channels for an adequate collateral circulation from the vessels of the pericardium.

Wearn,[11] studying the anatomy of the Thebesian vessels in human hearts, revived the Thebesian back flow hypothesis of Pratt and concluded that "in the event of gradual closure of the orifices of the coronary arteries the Thebesian vessels can supply the heart muscle with sufficient blood to enable it to maintain an efficient circulation."

In 1930 Leary and Wearn[12] reported two cases of complete chronic occlusion of both coronary arteries at their orifices and concluded: "The only adequate explanation of the ability of these patients to live and work rests upon a belief that the Thebesian veins have supplied the compensatory circulation necessary for the functioning of the heart muscle."

In 1932 Moritz, Hudson and Orgain[13] reported the findings in four human hearts with partial or complete obliteration of the pericardial sac by fibrous adhesions in which the coronary arteries had been injected with a colloidal suspension of lampblack and anastomoses were found to exist traversing the adhesions between the heart and pericardium. This was an anatomical demonstration of the acquired extracardiac vascular anastomoses suggested by Thorel.

3. *Early Studies in the Surgical Laboratory*

Experimental studies were begun by Claude S. Beck in February of 1932 in an attempt to produce adhesions between the heart and other tissues for the purpose of providing a collateral vascular bed as a source of collateral circulation to the myocardium. The work was suggested by the demonstration of Moritz, Hudson and Orgain of anastomotic vascular channels in adhesions between the heart and pericardium. Tichy and Moritz joined as collaborators in these first experimental studies the results of which were published in 1935.[1, 14]

In this work it was clearly demonstrated that vascular connections could be produced between coronary and extracoronary vessels. The more exact nature of the vascular connections were not determined in these earliest studies. The procedure appeared at this time to protect the heart but no precise method of measuring the degree of protection had been worked out. However, as a result of this work an idea was born demonstrating the feasibility of a surgical procedure for the purpose of improving the blood supply to the myocardium. Thus was opened a new field for study in the domain of biology and medicine.

Harold F. Robertson[15] in 1934 published the results of some studies in which he attempted to ligate the main venous channels of the heart in one to three stages and later attempted to ligate all the coronary arteries in several additional stages. He observed that "when animals were reoperated and adhesions separated there was much hemorrhage, the underlying heart became cyanotic and appeared to be nourished by the adhesions." He concluded that these experiments showed that the " myocardial nutrition distinctly depends upon the vessels contained in the adhesions." This conclu-

sion was a matter of opinion since there were no controlled statistical data to support the opinion and no anatomical studies of the condition of the vascular system as altered by the procedure. Regarding any possible beneficial effect of venous ligation he later concluded that the "myocardial changes produced would not prove beneficial to a heart already suffering from other pathology."[16]

All of the earlier experiments pointed to the need of a better understanding of collateral circulation in the heart. However, at this date there was still the maximal diversity of opinion about collateral circulation in the normal heart and in fact there were no anatomical or physiological studies to indicate that a collateral circulation does develop in response to arterial occlusion. New methods of study were needed to test the various and conflicting ideas about collateral circulation to the myocardium. The laboratory studies were continued and in 1936 additional anatomical information was published.[17]

In these studies chronically occluded coronary arteries of the dog heart were injected with barium sulfate gelatin mixtures according to the method of Louis Gross. This method did not visualize capillaries and veins as did the water solution of iron ferrocyanide (Prussian Blue) used in the previous experiments. The barium sulfate gelatin mixtures passed through arterioles with difficulty or not at all if they measured less than 70 micra in diameter in the histologic sections of the injected heart.

As a result of these studies two phenomena were clearly demonstrated, it is believed for the first time in the mammalian heart: (1) The identification of newly formed arteriolar connections between coronary artery system and the internal mammary system. These were found in preparations in which the substernal muscles with the associated mammary arteries had been detached from the sternum, sutured to the surface of the abraded heart and the coronary vessels constricted. The anastomoses were large enough to permit free passage of the barium gelatin mixture. The ability to obtain such anastomoses was limited to a small percentage of the preparations, presumably due to the difficulty of obtaining the optimum conditions for the development of such a collateral circulation. When obtained the collateral injection flow passed with sufficient ease to fulfill Pratt's postulate that the anastomosing vessels probably serve as a pathway for functional collateral circulation.

(2) The demonstration of tremendous enlargement of anastomotic channels between chronically occluded coronary arterial segments and unoccluded coronary arteries. These vessels could be identified by their increased diameter and tortuosity, indicating increase in length as well as in diameter. Histologically they bore no resemblance to the arteriole normally found in the same situation, being lacking in smooth muscle and elastic tissue. By dissection they could be shown to connect coronary arteries. These vessels were shown to measure as much as 14 times the maximum diameter of normal intercoronary anastomoses.

The results of these studies were again of an anatomical nature and did

not answer the question as to the specific role of a surgical procedure in augmenting collateral coronary circulation. The hypothesis that intercoronary communications might provide collateral circulation seemed to be proved by the great enlargement of these anastomoses. Furthermore, the mathematics of fluid flow in tubes would indicate that the per second volume flow through a collateral vessel varies as the (diameter)^4, other factors being constant. This gives a considerably greater significance to the observed enlargement of the anastomotic channels. The observations reported in this study "suggest the possibility that there may be a chemical or metabolic factor elaborated in the ischemic area which exerts an influence on adjacent arterial anastomoses."[17]

In 1940 Burchell[18] confirmed the enlargement of collateral channels bridging around chronic arterial obstruction placed below the primary branches of the main coronary arterial divisions in dogs. Basal anastomoses were demonstrated without difficulty but in his experiments any flow through tissue adherent to the epicardium was thought to be minimal or non-existent. He pointed out that the theory of reestablishment of cardiac function after healing of an infarct had not been stressed since the work of Hirsch and Spalteholz in 1907.

4. *Confirmatory Studies in the Human Heart*

In 1938 Monroe J. Schlesinger[19] published information gained from injection studies of human hearts showing that as in the dog heart anastomoses enlarge as a result of stenosis or occlusion of major coronary arteries. Age alone was not established as a factor causing enlargement as had earlier been suggested by Gross. By a continuation of the same method of study and analysis a significant new finding was described in 1951 by Zoll, Wessler and Schlesinger[20], namely, that in the absence of arterial disease in the heart that significant enlargement of intercoronary anastomoses occurs in chronic anemia, chronic pulmonary disease with cor pulmonale, cardiac hypertrophy, and valvular heart disease. It was concluded that cardiac hypoxia was common to all these conditions and this was regarded as the probable stimulus causing the enlargement of the intercoronary anastomoses.

This work led Blumgart et al[21] to restudy experimentally the development of collateral circulation in the dog and later in the pig. They were of the opinion that the arterial anastomoses in the normal pig heart were more nearly comparable with those in the normal human heart as to size and distribution. The anastomoses of the normal dog heart were shown to be slightly larger. They reached the same conclusion as had been previously reported[17] that chronic severe arterial narrowing leads to enlargement of intercoronary anastomoses, most readily demonstrable 12 days or more after the arterial obstruction although in some specimens noted at an earlier time.

Gregg et al[2] had previously shown that significant increase in collateral flow frequently begins in the first 48 hours after an acute arterial occlusion.

5. *Physiological Studies of Collateral Coronary Circulation*

Let us return to the viewpoint of the physiologist. Tennant and Wiggers[22] in 1935 noted that after ligation of a main coronary artery in the normal dog heart that the blood supply is so far reduced that contraction in the ischemic area invariably fails within one minute and Wiggers and Green[23] state that this phenomena cannot be prevented by drugs that elevate aortic pressure or act upon collateral vessels.

Gregg, Green and Wiggers[24] studied the pressure in coronary arteries distal to a ligature and found a pressure to be maintained at roughly one fifth of aortic pressure. From an analysis of the peripheral coronary pressure curves they concluded that the principal systolic rise was due to squeezing of the isolated arterial system by the ventricular contraction beginning in the isometric phase, rather than the result of transmission of blood and pressure through collaterals from sources approximating aortic pressure. They noted however that a "very small amount" of arterial blood bleeds back from the periphery of a divided coronary artery.

Stella[25] in 1932 was unable to record any flow from the peripheral end of a divided coronary artery when all the other coronary arteries were briefly centrally occluded, indicating rather decisively that what backflow is present comes from other arteries. Wiggers[26] reviewed his data on the question of collateral blood supply available to the myocardium and concluded: "When critically reviewed most of the experimental evidence favors the view that from a practical aspect the coronary branches are essentially terminal; anastomoses such as exist in normal hearts apparently have no functional value." However, Wiggers also said, "The existence of negligible collateral supply in normal hearts does not preclude the enlargement of minute potential communications nor the development of new ones when a main branch (of a coronary artery) is slowly occluded." Before writing this opinion Wiggers had seen a heart[27] from the Beck laboratory in which an area of the myocardium to which the supply artery had been chronically interrupted was seen to be again vigorously contracting. Wiggers then offered the suggestion that the stimulus that might cause this hypothetical enlargement of collateral channels to be a "differential of pressure" between occluded arterial segments and sources of collateral blood supply.

6. *Physiological Demonstration of Increased Intercoronary Collateral Circulation*

Following the anatomical demonstration of enlargement of intercoronary anastomoses in 1936,[17] some preparations were made in the Beck laboratory in which coronary arteries in the dog were chronically occluded and myographic studies were made of the surface of the heart over an area originally supplied by the occluded artery as well as peripheral coronary pressure records and backflow measurements from the chronically occluded arteries.[28] Great increase in the peripheral coronary artery pressure at times approximating aortic pressure, and backflow measurements in amounts as much as 25 times expected in the normal were observed after chronic coronary arterial obstruction. This conclusively demonstrated by an objec-

tive method and for the first time "that following chronic occlusion of a major coronary arterial ramus that there develops a massive new collateral circulation capable of again supporting myocardial contractions."

Attempts were made to trace the source of this collateral.[29] This proved to be difficult, but gave the following information: Two-thirds to nine-tenths of the blood coming into a chronically occluded arterial segment could be definitely shown to come from the unoccluded coronary arteries. It was not possible to accurately determine the source of one-tenth to one-third of the collateral except that the quality of the blood was indistinguishable from arterial blood on the basis of oxygen and carbon dioxide content. Some of it no doubt came from the septal artery and the remainder from extracardiac sources. These findings are in complete agreement with the anatomical studies showing great increase in intercoronary collaterals and only slight increase in extracardiac anastomoses.[17]

7. *The Surgical Problem of Augmenting Collateral Coronary Circulation*

A. Abrasion of heart and pericardium

Getting back to the surgical problem, the most urgent task seemed to be to work out a method of accurately measuring the benefit of a surgical procedure designed to improve collateral coronary circulation.

A carefully controlled statistical study of mortality and infarction following a standard descending ramus coronary artery ligation was carried out. The results, in normal dogs were compared with the same ligation in animals that had previously been prepared by mechanical abrasion of the surface of the heart with a specially designed mechanical burr with removal of considerable amounts of epicardium.[30]

The results of this study showed a 70 per cent mortality in the normal animals and a 38 per cent mortality in the prepared animals when the descending branch of the left coronary artery was ligated at its origin one to three weeks after the abrasion. Key et al[31] later had a comparable mortality of 73.3 per cent in an adequate series of descending ramus ligations in normal animals and found that previous removal of the epicardium and the application of a pedicle graft of jejunum from which the mucosa was removed reduced the mortality from the same ligation to 6.9 per cent. Even though the mortality following surgical ligation of a coronary artery depends upon many biological variables and therefore may not be the same in every laboratory or in the same laboratory, under altered circumstances, it is believed that the lowered mortality observed in the above mentioned studies, represent a significant difference in the behavior of the two groups of animals. This indicates clearly that previous abrasion protects the heart against acute coronary obstruction. In the latter experiments of Key et al proof must still be supplied that the pedicle graft is supplying a significant amount of blood to the ischemic myocardium.

B. Coronary sinus ligation

A variation of the retroperfusion of the coronary sinus was suggested by Gross and Blum[32] i.e. ligation of the coronary sinus. Their studies sug-

gested that coronary sinus ligation prior to left descending ramus coronary artery ligation reduced the amount of resulting infarction. Post mortem injection studies of the unoccluded arteries with barium sulfate gelatin mixtures showed better filling of the occluded arterial segment under the following circumstances: 1. After coronary sinus ligation alone or 2. After coronary sinus ligation followed by later descending ramus coronary artery ligation. These studies indicated that enlargement of intercoronary anastomoses occurred following coronary sinus ligation. It was their impression that coronary sinus ligation prior to coronary artery ligation reduces the amount of infarction, but the published data does not supply adequate proof of this impression.

In 1938 Gregg and Dewald[33, 34] showed in acute experiments that ligation of the coronary sinus greatly increases the pressure within the veins of the left ventricle to values approaching mean aortic pressure. Also that this procedure limits left coronary artery inflow mildly to considerably, and causes a marked increase in the retrograde flow from the periphery of a divided coronary artery. The retrograde blood was found to be very dark and to contain only approximately three volumes per cent of oxygen. They observed that coronary sinus ligation did not prevent the abrogation of myocardial contractions following coronary artery occlusion.

In July of 1941 Beck and Mako[35] published the results of a study, that was adequately controlled, in which it was determined that if the coronary sinus is ligated several days to four months before descending ramus coronary artery ligation the mortality from the latter procedure is reduced from 70 per cent in the controls to 50 per cent and the size of the infarcts was reduced in the survivors that had previously had coronary sinus ligation. However, it was concluded that further studies should be done before considering this as a therapeutic measure in clinical coronary disease.

C. Acute arterial retroperfusion of the coronary sinus

In 1943 Roberts, Brown and Roberts[36] studied the effect of acute retroperfusion of the coronary sinus of the dog's heart with arterial blood at aortic pressure. The principle was the same as had been shown by Pratt to restore a coordinated beat in the isolated non-working cat heart. They reported that the dog heart will continue to beat regularly and forcefully after extensive obstruction of coronary arterial inflow. No statistical comparison was made of the behavior of the heart with the arterialized coronary sinus as compared with the normal heart to prove their contention, but it was their reported impression that there was a striking protection against the immediate and early effects of acute coronary artery obstruction.

D. Chronic arterialization of the coronary sinus.

If the perfusion of the coronary sinus with arterial blood supplies a collateral circulation that protects the heat in acute laboratory experiments, Beck's contention would seem quite logical that chronic arterialization by anastomosis of a systemic artery to the coronary sinus might be of value in providing a more abundant collateral circulation than either coronary sinus ligation or abrasion of the epicardium. Such a procedure was de-

veloped in the Beck laboratory and tested by the coronary artery ligation mortality and infarction test.[37]

A technique was developed to arterialize the sinus by using a vein graft to bring arterial blood from the aorta to the coronary sinus. At a second stage the coronary sinus was narrowed to 2 or 3 mm. in diameter between the entrance of the shunt and the ostium in the right auricle. The technique was perfected to a degree that this could be done without the development of thrombosis, a complication which was a considerable problem in the earlier attempts. In testing the benefit of this procedure by descending ramus ligation a 70 per cent mortality was obtained in the control animals and only a 20 per cent mortality in the animals in which the vein graft was patent and feeding arterial blood retrograde into the coronary venous system which normally drains into the coronary sinus. As this test of benefit was extended to a larger series the mortality following descendens ligation was found to be 8.9 per cent in a series of forty-five animals.[38]

E. The Mechanism of Protection of Arterial Retroperfusion of the Coronary Sinus

That this protection was due to increased collateral circulation was indicated by the actual measurement of increased collateral circulation by the backflow method previously described.[28] After arterialization of the coronary sinus there was found an immediate increase in the backflow from the divided coronary artery.[39] The backflow during the first five to 12 weeks after production of the shunt was found to be blood only partly saturated with oxygen, indicating that it has passed through a capillary bed prior to entering the artery. During the above mentioned time interval clamping the shunt reduces the backflow. Beyond the five to twelve week interval the backflow was found to remain increased, to be again arterial in character and to be unaffected by clamping the shunt in either the amount of backflow or in the degree of arterialization of the blood. Intercoronary anastomoses were found to have increased in size while gradual sclerosis had taken place in the small veins of the outflow tract of the arterialized coronary sinus. The venous sclerosing process gradually reduced retrograde flow through the myocardial capillaries until eventually all physiological contact is lost between the arterialized sinus and the myocardia capillaries.[40]

Early after arterialization the retrograde flow offers protection against ventricular fibrillation when a coronary artery is ligated. This might be due to other factors than improved capillary blood flow in the ischemic myocardium but the marked reduction in the degree of infarction can only be interpreted as the result of improved collateral circulation.[38, 41-45] The protection is much more striking than after simple coronary sinus ligation and has been observed to be present for one year.

Eckstein et al,[46] by acute arterial perfusion studies, supplied the proof that was lacking in the Roberts' report regarding the beneficial effect of acute arterialization of the coronary sinus in acute coronary artery occlusion. In control animals a 70 per cent mortality in one hour was found after

ligation of the circumflex artery, all the fatalities were due to ventricular fibrillation occurring within 10 minutes after the occlusion. In a second group with the coronary sinus arterialized at 50 mm Hg. pressure all survived for one hour. Eckstein and Leighninger and co-workers[39] discovered that the increased collateral provided in both the acute and chronically arterialized coronary sinus often prevented the maximal S-T deviation in the electrocardiogram after acute coronary arterial occlusion. In the animals with functioning shunts 75 per cent showed evidence of protection as compared with 25 per cent of a group of normal dogs. This per cent increased incidence of evidence of protection was present early after the sinus arterialization and also after late blood flow had ceased from the arterialized venous system to myocardium. The late protection was correlated with the increased intercoronary collateral flow.

Further light was cast on the modus operandi of the arterialization of the coronary sinus by evaluating the effect of a sham operation in which the complete arteriovenous shunt operation was done, but the shunt was ligated at the completion of the procedure.[40] There was a definite increase of the retrograde circumflex flow averaging 6.9 cc./min. four to five weeks after the initial procedure as compared with 3.8 cc./min. in normal dogs. In these experiments no constriction of the coronary sinus was produced between the shunt and the ostium of the coronary sinus.

In the animals with A-V shunts and the coronary sinus opening narrowed to an external diameter of 2-3 mm., backflows of 11.0 cc. per minute were found after a comparable time interval. The increased backflow in the sham operations represents the dilating effect of the trauma of operation, comparable to the abrasion experiments, on the intercoronary anastomoses. Lesser degrees of trauma, as pericardiotomy and resuscitation from ventricular fibrillation do not always cause dilation of the intercoronary anastomoses.

Unfortunately the technical aspects of the chronic arterialization of the coronary sinus and the fact that the residual arteriovenous shunt introduces an added strain on the heart, impose limitations on the clinical application of this procedure and suggest the desirability of going back to a simpler procedure for clinical use.

F. Implantation of internal mammary artery into myocardium

Vineberg[47, 48] has confirmed the production of new extracardiac anastomoses by reporting the production of vascular communications between the internal mammary artery and the coronary vessels in over 50 per cent of preparations by placing the internal mammary artery in a myocardial tunnel and allowing it to bleed from the origin of the sixth intercostal artery into the tunnel. Vineberg is of the opinion that the blood flowing from the internal mammary does not lead to the formation of a hematoma within the myocardium, but that it finds its way almost immediately into the myocardial sinusoids and establishes a new circulation. Permanent vascular connections were shown to develop between mammary implant and both the coronary arterial and venous systems in a high percentage of prepara-

tions. Physiological studies showed that blood could be perfused, under constant pressure equal to the mean aortic pressure, into the coronary vascular system through an implanted internal mammary artery at the rate of 45 cc. per minute. Retrograde flow from the periphery of the implanted internal mammary artery in the living animal was found to be of the order of one cc. per minute. One of the most interesting findings was the development of intimal thickening in practically all the implanted arteries, the degree of which appeared to be inversely proportional to the flow in the vessel, and caused almost complete obliteration of the lumen in the end of the vessel where there was no flow.

On the basis of backflow, vascular injections and erosion preparations it appears that these anastomoses are about the same size as the largest intercoronary anastomoses occurring in the normal heart. On the basis of existing knowledge it would appear that the contribution of blood through these implanted internal mammary arteries is small compared with the collateral from other coronaries. However, such a contribution from extracardiac sources could become more significant as the total coronary arterial inflow becomes progressively reduced. It is doubtful that this would be the case with only one major coronary arterial ramus obstructed. Evidence is presented in the constant pressure perfusion experiments that some of the perfused blood passes through myocardial capillaries. There have been no measurements to indicate whether or how much blood may be shunted through arteriovenous communications that have been shown to develop under these circumstances. The crux of the matter lies in measuring the amount of blood that mammary artery implants contribute to chronically occluded arteries, as compared with the collateral from other coronary arteries. Such studies were carried out by Leighninger[43, 44] who found no increase over the normal backflow in these preparations and no measurable component contributed to the backflow from the implanted internal mammary artery. The implanted artery was patent in fifteen of twenty dogs studied. It is conceivable that the operation of implanting the internal mammary artery under different circumstances could stimulate the development of intercoronary collaterals.

G. Abrasion of Heart and Pericardium, Chemical Irritation and Partial Coronary Sinus Obstruction

Studies were again undertaken to evaluate the stimulation of collateral circulation by the simpler procedures of mechanical abrasion of the heart and pericardium, the use of chemical irritants, and partial coronary sinus obstruction.[38, 43, 44] By this time it had become apparent from the studies in the normal control animals that the findings were contrary to the hypothesis of Pratt[8] and others and also of Wiggers[26] who said, "From a practical aspect the coronary branches are essentially terminal; anastomoses such as exist apparently have no functional value." For in sixty-five normal dogs studied the circumflex backflow varied greatly and measured from 0.4 to 21.0 cc. per minute; the median was 2.8 cc./minute and the average 3.8 cc./minute. The mean peripheral coronary pressure varied from 1/14 to 3/10 of the mean aortic pressure.[40] When the electrocardiogram was

studied it was noted that in 20 per cent of normal dogs in the area of the greatest backflow that the maximal change in the S-T segment did not develop following simple circumflex occlusion, but that the maximum change did take place when the distal artery was opened and allowed to bleed back.

The failure of complete infarction of the supplied myocardium can now be explained as *due to intercoronary collateral and nothing else.* To date there have been no physiological observations to indicate that any collateral circulation occurs via the minute corrections between the terminal branches of the coronary arteries and the cardiac chambers in the normal heart or after chronic arterial obstruction. Pressure relationships would be favorable for such a flow from the left ventricle to the coronary artery during systole only when the coronary artery pressure is reduced significantly below aortic pressure. Any flow from the right ventricle into coronary arteries could occur only under the abnormal circumstances in which right ventricular pressure considerably exceeds intracoronary and intramyocardial pressure during systole.[26, 49] Furthermore, no anatomical studies have to date revealed any enlargement of possible collateral channels from intracardiac sources in the presence of chronic arterial obstruction. It would seem that great enlargement of these channels would be necessary before a to and fro flow of this nature could possibly reach the myocardial capillaries, since the resistance to flow through the normal sized channels into occluded coronary arteries appears to be great.

In 41 dogs subjected to mechanical abrasion of the heart and parietal pericardium, the application of 0.2 gram of powdered asbestos and narrowing of the coronary sinus to a diameter of 2 to 3 mm., the average circumflex backflow was found to be 8.5 cc. per minute varying from 0.4 to 26 cc. per minute. Furthermore, 68 per cent of the dogs showed electrocardiographic evidence of protection.[43, 44] What makes these experiments more significant and crucial is the fact that *increased collateral was produced in the absence of arterial obstruction.* Descending ramus ligation after preparation by this procedure resulted in a 26.6 per cent mortality in a group of 30 dogs as compared to 70 per cent in the control group of normal animals. In other words, the increased circumflex backflow provided by the procedure, while amounting to only 4.7 cc. per minute indicating approximately double the normal intercoronary collateral, represents the lifesaving factor in 43 per cent of the animals so prepared. And what is equally important this small increment in collateral saves much myocardium that would otherwise be converted into the scar tissue of infarction. The increase in basic collateral saved life and myocardium. After the acute occlusive episode there is the opportunity for the continued gradual enlargement of anastomotic channels so that maximal function can again be restored in the ischemic myocardium. Gregg and Sabiston[50] have estimated that in a heart with an acutely ligated coronary artery the oxygen supply to the potentially infarcted zone is 3 per cent of the normal. After the above outlined surgical procedure the potential supply would be increased to about 7 per cent of the normal requirement. When we study the

over all picture we are impressed by the narrow margin between life and death in an acute coronary arterial occlusion, and how important it is that a little blood continue to flow into the ischemic myocardium. The fact that infarction is significantly reduced[42] is ample proof that the increase in collateral flow as observed in the backflow studies provides for sufficient flow in the myocardial capillaries to maintain the viability of muscle fibers that would otherwise undergo necrosis. This represents one of the ultimate tests of benefit that can be applied to the procedure.

Thompson[51] has advocated a procedure first suggested by Beck in 1936[52] of simple pericardiotomy and introduction of a powdered foreign body irritant into the pericardium. Beck used powdered beef bone and Thompson has used powdered magnesium silicate (U.S.P. Talc). Backflow studies after the Thompson procedure have shown a slight increase in average backflow but considerably less than the combined procedure described above.[43] However, Thompson et al have reported good clinical results from this procedure in a rather large series of patients.[53]

To date there is no crucial laboratory data on the effectiveness of the combined stimulus provided by the surgical procedure plus the simultaneous factor of chronic narrowing of the coronary arteries. The fact that the clinical results seem better than one might expect from the study of the relatively acute backflow experiments suggests that the benefit to collateral blood flow may be magnified by an already existing reduction in arterial inflow.

8. Metabolic Factors Operative in the Augmentation of Collateral Coronary Circulation

The studies that have been discussed naturally arouse curiosity concerning the fundamental biological factors that cause interarterial anastomoses to enlarge. It has been common to employ the teleological assumption that a need for blood stimulates the enlargement of collateral channels. Although this might be true in a sense it should be possible to identify the factors be they physical or metabolic responsible for the vascular architectural change that lead to this rather enormous enlargement of collateral channels.

Wiggers has emphasized the possible importance of a differential of pressure between arteries as a stimulus to collateral development. In our previously reported studies[17, 28] there were two instances in which there was complete infarction of the parts of the wall of the right ventricle supplied by the acutely occluded right coronary artery with conversion into scar tissue. Although the right coronary artery was in each case patent distal to the occlusion, the backflow and peripheral coronary pressure in one were exceedingly low, the backflow being 0.1 cc./minute. Significant enlargement of intercoronary anastomoses was absent in both by injection studies. In these instances in spite of a wide differential of pressure existing for many months no enlargement of collateral channels had taken place. Indeed, such a finding is perfectly reasonable since the metabolic requirements of scar tissue must be much lower than functioning myocardium. It

is believed and has been previously suggested[17, 54] that factors within an ischemic zone of myocardium influence blood flow into the ischemic zone perhaps first by a reversible *pharmacological dilation* of anastomoses which lowers resistance to flow and that the subsequent permanent *anatomical enlargement* of the collateral channels may be secondary to the physical effects of *flow* within the collateral rather than the mere pressure differential. In the earlier reported studies of the development of intercoronary collateral following chronic arterial occlusion,[17] treadmill exercise was given to some of the animals with constriction of coronary arteries with the belief that increased work of a segment of myocardium distal to a narrowed artery would be the physiological equivalent of temporarily increasing the degree of ischemia distal to the arterial narrowing and that this would serve as an added stimulus to the further development of collaterals. The collateral enlargements were successfully produced but the specific role of the exercise was not determined in these studies. More recently, using the same treadmill, Eckstein[55] has shown that when dogs with narrowing of a coronary artery are exercised they develop significantly more collateral than control animals that receive no exercise. Further studies into the chemistry and pharmacology of inflammation and of myocardial hypoxia may further elucidate and explain specific mechanisms involved. The findings of Zoll et al[20] and others[56, 57] of enlargement of intercoronary anastomoses in the absence of coronary arterial disease in chronic anemia, valvular disease, cardiac hypertrophy and cor pulmonale with pulmonary fibrosis fits well into such a concept. Eckstein[56] has shown that the enlargement of intercoronary channels that occurs during four weeks of severe anemia in experimental animals disappears following correction of the anemia, being yet in the reversible phase. It is probable that this represents principally the pharmacological effect of metabolites and that if the anemia were sufficiently prolonged that permanent anatomical changes would take place that would not be reversible.

SUMMARY AND CONCLUSIONS

The anastomoses between coronary arteries present in the normal heart provide a basic collateral circulation, which while not sufficient to maintain myocardial contractions following acute interruption of the normal arterial supply, generally enables the survival of variable amounts of myocardium providing death of the individual does not follow the occlusion. In the survivors there is a gradual enlargement of collateral circulation quite variable in amount but sufficient to enable the ischemic myocardium to again regain its contractile ability. The collateral blood comes exclusively from other arteries. The nearest artery or the anatomically shortest path of least resistance appears to be the commonest source and route. In the early phase of the reduction of coronary arterial inflow the majority of the collateral is supplied by other coronary arteries. If and when it is possible to reduplicate the experiments of nature and completely interrupt all the normal arterial inflow to the myocardium with survival, it should be possible to trace and measure the blood flow from the extracardiac arterial sources.

The surgical procedure of abrasion of the epicardium, coronary sinus constriction and the application of a mild chronic chemical irritant (powdered asbestos) to the heart significantly increases the basic collateral circulation available to the myocardium. This increase in basic available collateral has been noted to persist for at least one year and has been shown to significantly lower the mortality and myocardial destruction following acute arterial occlusion.

The exploration of the application of these principles in the treatment of coronary disease in man would appear to be axiomatic. The principle of improving the collateral circulation to the myocardium must be the sine qua non of our search for a better treatment of coronary disease until such time as the arteriosclerotic process can be prevented or arrested.

The ultimate precise measure of benefit in man will depend upon the comparison of similar groups of treated and untreated patients with disease of the coronary arteries. In spite of pessimism such as has been voiced by Blumgart and Paul,[58] to find an answer to the question of benefit in man should not be exceedingly difficult for good clinicians who view the biological problem objectively. A careful plan of preoperative study of patients and an adequate system of follow-up will in time yield a precise answer. No doubt much is yet to be learned but the evidence at hand indicates that a firm foundation has been established for improving collateral circulation to the myocardium by surgical methods.

RESUMEN Y CONCLUSIONES

Las anastomosis entre las arterias coronarias que existen en el corazón normal proporcionan una circulación colateral básica que si bien es insuficiente para mantener las contracciones cardiacas después de una repentina interrupción del aporte sanguíneo normal, generalmente permite la sobrevida de variables volúmenes del miocardiocuando la oclusión ne es seguida de muerte inmediata.

En los supervivientes hay un gradual aumento de la circulación colateral muy variable en volumen pero suficiente para permitir que el miocardio isquémico recupere su contractibilidad. La sangre colateral viene exclusivamente de otras arterias.

La arteria más próxima o la senda anatómica más corta y de menor resistencia parece ser la fuente provisora. En la fase temprana de la reducción del aflujo sanguíneo la mayoría de la sangre es proporcionada por las otras coronarias. Cuando sea posible imitar la experiencia e interrumpir completamente todo el aflujo sanguíneo arterial normal del miocardio con sobrevida, será posible estimar y calcular el aflujo sanguíneo que provenga de fuentes arteriales extracardiacas.

El procedimiento quirúrgico consistente en la abrasión del epicardio, la constricción del seno coronario y la aplicación de irritantes químicos moderados (polvo de asbesto) al corazón aumenta el aporte sanguíneo colateral del miocardio. Se ha notado que este aumento circulatorio persiste por lo menos un año y ha hecho descender notablemente la mortalidad y el daño al miocardio después de la oclusión arterial.

La exploración de la aplicabilidad de estos principios en el tratamiento de la enfermedad coronaria en el hombre parecería axiomática.

Hasta que el proceso arterioescleroso pueda ser evitado o detenido es preciso buscar los métodos que mejoren la circulación del miocardio. La estimación del valor de los métodos depende de la comparación de grupos tratados y no tratados. A pesar del pesimismo mostrado por Blumgart y Paul (58) no es difícil llegar a una respuesta si los buenos clínicos observan el problema biológico objetivamente.

La observación previa y posterior a la cirugía rendirán una respuesta precisa. No hay duda que falta mucho por lograrse para mejorar la circulación colateral del miocardio.

RESUME

Les anastomoses entre artères coronaires dans le coeur normal permettent une circulation collatérale de base. Elle est insuffisante à maintenir les contractions myocardiques à la suite de l'interruption brutale du débit artériel normal. Toutefois, elle permet généralement la survie d'un territoire variable du myocarde, si la mort n'a pas immédiatement fait suite à l'occlusion. Chez les survivants, il y un accroissement progressif de la circulation collatérale, assez variable en quantité, mais suffisante pour permettre au myocarde ischémique de retrouver sa capacité contractile. Le sang collatéral vient exclusivement des autres artères. L'artère la plus proche ou la voie anatomiquement la plus courte et où il y a le minimum de résistance en sont l'origine la plus commune.

Dans la phase précoce de réduction du débit artériel coronaire, la plus grande partie de la circulation collatérale est fournie par les autres artères coronaires. Quand il sera possible de reconstituer l'expérience que nous offre la nature, en interrompant complètement tous les apports normaux de sang artériel au myocarde, tout en maintenant la survie, on devrait arriver alors à mesurer le débit sanguin à partir de ses sources artérielles extracardiaques.

Le procédé chirurgical de l'abrasion de l'épicarde, la constriction du sinus coronarien, et l'application sur le coeur d'un irritant chimique permanent à action douce (amiante en poudre) accroit considérablement la circulation collatérale destinée au myocarde. On a noté que cette augmentation persistait pendant au moins un an, et permettait une diminution considérable de la mortalité et de la lésion myocardique consécutive à l'occlusion artérielle aiguë.

L'application de ces principes au traitement des affections coronariennes chez l'homme devrait se présenter comme un axiome. L'amélioration de la circulation collatérale du myocarde doit être l'élément "sine qua non" de nos recherches sur le traitement de l'infarctus du myocarde tant que nous ne serons pas arrivés à éviter ou à freiner le processus d'artériosclérose.

Le seul moyen précis d'en mesurer l'avantage chez l'homme consistera à comparer des groupes semblables de malades atteints d'affections coronariennes, les uns ayant subi le traitement, les autres ne l'ayant pas subi.

Malgré le pessimisme de Blumgart et Paul, une réponse à la question de savoir si un tel procédé est avantageux pour l'homme ne devrait pas comporter de difficultés excessives pour de bons cliniciens qui voient objectivement le problème biologique. Un plan soigneux d'études pré-opératoires des malades, et un système convenable de contrôle doit fournir una réponse en temps voulu. Il n'y a aucun doute qu'il reste beacoup à apprendre, mais nous avons la certitude de posséder une base solide qui nous permet d'améliorer les troubles de la circulation collatérale par des procédés chirurgicaux.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Die im normalen Herzen bestehenden Anastomosen zwischen Koronararterien gewährleisten die Basis eines collateralen Kreislaufes, der—obwohl nicht ausreichend für die Aufrechterhaltung von Herzmuhkel-Kontraktionen nach akuter Unterbrechung des normalen ateriellen Zuflusses—im allgemeinen das Überleben variabler Teilstücke des Myocards ermöglichen, sofern der Tod des Individuums nicht auf den Verschluss folgt. Bei dem Überlebenden kommt es zu einer schrittweisen Zunahme der collateralen Zirkulation, die in ihrer Stärke ziemlich schwankt, aber ausreicht, um dem ischemischen Myocard zu ermöglichen, sein kontraktiles Vermögen wieder zu gewinnen.

Das kollaterale Blut stammt ausschliesslich aus anderen Arterien. Die nächstgelegene Arterie oder der anatomisch kürzeste Weg des geringsten Widerstandes dürfte für gewöhnlich der Ursprung und der Verlauf sein.

Während der ersten Phase der Herabsetzung des Koronararterien-Zustromes wird die Mehrzahl der Kollateralen durch andere Koronararterien versorgt.

Im Falle es möglich wäre, die Experimente der Natur zu wiederholen und den gesamten normalen arteriallen Zustrom zum Myocard vollständig zu unterbrechen, ohne dass der Tod eintritt, müsste es auch möglich sein, den Blutstrom extracardialer arterieller Herkunft zu verfolgen und zu messen.

Das chirurgische Verfahren der Epicard-Abrasio, Verengung des sinus coronarius und der Gebrauch eines milden chronischen chemischen Reizmittels—Abest-Puder- verbreitert die Basis für den dem Myocard zur Verfügung stehenden Collateral-Kreislauf beträchtlich. Es wurde beobachtet, dass diese Verbreiterung der Basis der zur Verfügung stehenden Kollateralen mindestens 1 Jahr anhält, und es wurde gezeigt, dass die Mortalität und die Zerstörung des Myocards nach akutem arteriellem Verschluss beträchtlich verringert wurde.

Die Erforschung der Anwendung dieser Grundsätze bei der Behandlung von Koronarerkrankungen beim Menschen erscheint axiomatisch. Das Prinzip der Verbesserung der kollateralen Zirkulation für das Myocard muss so lange die conditio sine qua non unseres Bestrebens nach einer besseren Behandlung der Koronarerkrankungen sein, bis der ateriosklerotische Prozess verhütet oder zu Stillstand gebracht werden kann.

Der am Ende genaueste Massstab eines Nutzens für den Menschen wird abhängen von dem Vergleich ähnlicher Gruppen von Behandelten und nicht

behandelten Patienten mit Koronararterien-Erkrankung. Trotz des Pessimismus, so wie er von Blumgart und Paul[58] zum Ausdruck gebracht wurde, sollte eine Antwort auf die Frage des Nutzens beim Menschen nicht so überaus schwierig zu erlangen sein für gute Kliniker, die das biologische Problem objektiv sehen. Eine sorgfältig geplante präoperative Untersuchung von Patienten und ein ad aequates System der Nachfürsorge wird rechtzeitig eine genaue Antwortverschaffen. Ohne Zweifel ist bist dahin noch viel zu lernen, aber derzutage liegende Augenschein weist darauf hin, dass eine feste Grundlage erreicht worden ist, um auf chirurgischem Wege die kollaterale Zirkulation zu verbessern.

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The Tuberculin Reaction During Chemotherapy for Pulmonary Tuberculosis*

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Changes in the tuberculin reaction during the course of pulmonary tuberculosis have been a matter of considerable interest for many decades. There has emerged no uniform agreement as to the significance or utility of any observed variations in intensity of reaction nor indeed in which direction the alterations occur. Studies exist on changes during rest, collapse and surgical therapy and have become more numerous during the past decade since the advent of chemotherapy for pulmonary tuberculosis. Examination of the above studies, however, reveals a paucity of reports on combined chemotherapy in its effect on the tuberculin reaction, particularly those carried on for more than the initial few months after commencing treatment. The following study was therefore carried out to add some data on the above points.

Method and Material

From February 1954 through June 1954 all patients entering the Tuberculosis Service of the Veterans Administration Hospital, Augusta, Georgia, who were diagnosed as having active pulmonary tuberculosis with positive sputum, and who had not had previous chemotherapy were tuberculin tested before being started on chemotherapy.

Chemotherapy, which consisted of the common drug pairs (1) SM (streptomycin) gms. 1 b.i.w. plus PAS (para-aminosalicylic acid) gms. 4 t.i.d. (2) SM gms. 1 b.i.w. plus INH (isoniazide) 100 mgs. t.i.d. and (3) INH 100 mgs. t.i.d. plus PAS gms. 4 t.i.d. was allotted to patients primarily, but not entirely, on a randomized basis. Immediately before chemotherapy was begun the patients were tuberculin tested with PPD (Purified Protein Derivative) 1st strength dose 0.1 cc. (.0002 mgs.) intradermally into the flexor surfaces of both forearms. After 72 hours, 2 right angle diameters of the induration on both arms were measured and the mean of the four readings recorded to the nearest millimeter. The same method was carried out at monthly intervals for the first four months and then bi-monthly until a total of a year of chemotherapy had elapsed. Patients who left against medical advice, before completing at least four months of chemotherapy, were not included in the study.

The patients in this study were all males and were classified as follows:

(1) SM and PAS group: 19 cases (12 White—7 Negro). Eleven were far advanced cavity cases, six moderately advanced cavity cases and two minimal cases. Three patients were 20 to 29 years of age; six 30 to 39; three 40 to 49 and two 50 to 59; five were 60 or over. One patient was

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TABLE I

MEAN CROSS DIAMETER OF TWO TUBERCULIN TESTS DONE BEFORE STARTING CHEMOTHERAPY AND AFTER 12 MONTHS OF CHEMOTHERAPY. (1st Strength PPD)

	Size of Tuberculin Reaction (mm.)												
	0	1	2	3	4	5	6	7	8	9	10	11	12
Before chemotherapy	3	4	1		1				1	4	1	4	6
After 12 mos. chemo.				1	1	3	2		3	2	3	3	4

	13	14	15	16	17	18	19	20	21	22	23
Before chemotherapy	3	3	6	4	4	3					1
After 12 mos. chemo.	2	1	1	1		5			1		

followed for 4 months, one for 8 months, one for 10 months and sixteen for 12 months.

(2) SM and INH group: 10 cases (7 White—3 Negro). Four were far advanced; five moderately advanced and one minimal. Four were 20 to 29 years of age; one 30 to 39; two 40 to 49; two 50 to 59; and one 60 or over. One patient was followed for 4 months; two for 6 months; two for 8 months; one for 10 months and four for 12 months.

(3) INH and PAS group: 13 cases (8 White—5 Negro). Seven were far advanced; five moderately advanced and one minimal. Two were 20 to 29 years of age; six 30 to 39; two 40 to 49; two 50 to 59; and one 60 years of age or over. One patient was followed for 6 months, one for 8 months, three for 10 months and eight for 12 months.

(4) Mixed group: 7 cases consisted of patients who, during their period of chemotherapy, received more than one combination of drugs. Changes were made because of resistance, toxicity, or lack of response. These seven cases were all white, two were far advanced and five were moderately advanced. Two were 20 to 29 years of age; three 30 to 39; two 60 years or over. Two were followed for 8 months and five for 12 months.

Patients were treated on a modified bed rest regimen, and not all patients were available for testing at all designated times due to being on leave or pass. Thirteen of these patients received pulmonary surgery during this period of chemotherapy.

Analysis of Data

Table I shows the size of the tuberculin reaction in millimeters for all patients before being started on chemotherapy. Nine patients who did not react to 1st strength PPD or had less than 5 millimeters induration were classified as hypoergic. Table I also shows the size of the tuberculin reaction in those patients who completed 12 months of chemotherapy. It is to be noted that after 12 months of chemotherapy only two of the 33 cases would be considered as negative reactors to 1st strength PPD.

TABLE II

CHANGE IN SIZE OF TUBERCULIN REACTION (1st Strength PPD) UNDER CHEMOTHERAPY BY TYPE OF CHEMOTHERAPY AND DURATION OF TREATMENT

	TYPES OF CHEMOTHERAPY									
	SM & PAS					SM & INH				
Differences (in mm.) from prechemotherapy tuberculin readings — Mos. of chemo.	1	2	4	8	12	1	2	4	8	12
+20									1	
								1		
+18	1									
+15		1	2	1			2			
						1				
+10			1							
		3			1			1		
	1			1	1			1		
	1									
	3		1		1		1			
+ 5	1	1		1		1				
	2	3	1		2	1			1	
	4	1	1	1	1					
	1	1	1	1		1	1			
	1	2	2	1	1			2		
0	1	3	2	4	1	2	3		1	
		2	2	2	2	3				1
	2	1	3		2		1	1	1	
		1	1		1					1
	1			2						
— 5			1	3				1	1	1
				1				1		
					2				1	
			1		1	1	1			
—10										1
								1		
Mean of differences	+ 3.74	+ 3.05	+ 1.63	+ .11	+ .25	+ 1.10	+ 2.67	+ 1.56	+ .71	— 4.75
S.D. ±	4.90	4.51	5.94	4.99	5.19	4.95	6.90	9.17	9.27	3.86
t	3.34	2.93	1.20	.09	.20	.70	1.16	.48	.21	2.46
P.	<0.01	<0.01	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	<0.1 >0.05

S.D.—Standard Deviation

P.—Probability

TABLE II (Cont'd)

CHANGE IN SIZE OF TUBERCULIN REACTION (1st Strength PPD) UNDER CHEMOTHERAPY BY TYPE OF CHEMOTHERAPY AND DURATION OF TREATMENT

TYPES OF CHEMOTHERAPY																
IMH & PAS					Mixed					Totals				
1	2	4	8	12	1	2	4	8	12	1	2	4	8	12
													1	
												1		
										1				
											1	2	1	
		1									2	1		
		1										1		
1	1		1							2	1		1	
	1			1							1	1		1
2		1								2	3	2		1
			1							1		1	2	1
1										2				
		1								3	1	2		1
	1		3	1		1				2	3		4	1
		1						1		3	3	2	2	2
	3	1		1		1				4	5	2	1	2
2						1	1		1	4	3	2	1	1
	1	1	1		2			1		3	3	5	3	1
2		3	4	2	2	1	1	1		7	7	6	10	3
1	2				1		1	1		5	4	3	3	3
	1					1	1		1	2	4	5	1	3
1		1			1					2	1	2		2
1		1		1		1	1	1		2	1	2	3	1
1	1		1			1		1		1	2	2	6	1
		1										2	1	
			1	2					1				2	5
							1			1	1	2		1
									1					1
									1					2
					1			1		1		1	1	
							1					1		
+	+	+	+		—	—	—	—	—	+	+	+	+	—
2.25	2.45	2.69	1.92	0.0	1.86	.14	3.57	2.29	5.20	2.00	2.35	1.15	.41	1.24
5.49	4.88	6.01	5.14	5.95	4.26	3.67	4.91	4.88	5.07	5.32	4.99	6.63	5.82	5.41
1.42	1.68	1.62	1.28	0.0	1.22	.10	1.93	1.25	2.29	2.60	3.05	1.19	.46	1.31
>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	<0.1 >0.05	<0.05 >0.01	<0.01	>0.1	>0.1	>0.1

TABLE III

CHANGE IN SIZE OF TUBERCULIN REACTION UNDER CHEMOTHERAPY BY DURATION OF CHEMOTHERAPY FOR HYPOERGIC CASES

Difference (mm.) from prechemotherapy readings	Mo. of chemo.	1	2	4	8	12
	+20				1	
				1		
	+18					
	+15					
			1	2	1	
			2	1		
				1		
		2			1	
	+10		1			1
			1	1		
				1	1	1
		1				
		1	1			
	+ 5		1		1	
	4	1				
	2	1				
	0	2	1		2	
	— 1			1		
Mean of differences		+6.56	+8.75	+9.89	+8.29	+9.00
S.D.	+ —	5.95	4.82	6.35	7.36	1.42
t		3.31	5.15	4.66	2.99	9.00
P.		<0.05 >0.01	<0.01	<0.01	<0.05 >0.01	<0.1 >0.05

Table II shows the changes in the size of the tuberculin reaction one, two, four, eight and twelve months after starting chemotherapy as compared to the prechemotherapy measurements. The data is divided as to type of chemotherapy; and the mean of the differences, standard deviation, t-test,[1] and P (Probability) calculated. A probability of less than 0.05 but greater than 0.01 (underlined once) was considered as significant and one of less than 0.01 (underlined twice) was considered as highly significant. The data for all cases (totals) show that there was a significant increase in reaction one month after starting chemotherapy and a highly significant increase at two months. This significant increase is also present in the SM and PAS group. No significant changes in size are indicated in the SM plus INH, INH plus PAS and mixed groups. However, since both the t-test and probability (P) depend on the number of cases in each group, and since

the number of cases in these groups is small, all one can say is that there is no proven effect of chemotherapy on the tuberculin reaction of these groups, and that if larger groups are tested the changes, which parallel the SM and PAS group, might turn out to be significant.

Table III shows the changes in the hypoergic group (those with an induration of less than five millimeters to 1st strength PPD before treatment). Here again the patients are analyzed according to changes occurring one, two, four, eight and twelve months after chemotherapy. Highly significant increases occurred at the 2nd and 4th month and significant increases at one and eight months. Four of these patients were far advanced, four moderately advanced and one minimal. Seven were White and two Negro. Seven were under 50 years of age and two over 50.

Succeeding tables omit working data.

Table IV shows the data for the group as in Table II but excluding the hypoergic cases. When this is done, this subtotal group shows no significant changes in the tuberculin reaction except at 12th month where there is significant decrease in size of reaction. Each group analyzed separately shows no significant change except for the SM-PAS group where there is a significant increase at the 1st month and decrease at the 8th month. Again, as in Table II, the other groups are probably too small to yield significant data.

Table V. In order to make the groups of larger size and increase their value statistically, the cases were grouped and then analyzed according to those receiving SM (in combination with INH or PAS); INH (in combination with SM or PAS); and PAS (in combination with INH or SM). Analysis, according to this method, showed highly significant increase in the size of the tuberculin reaction at one and two month periods for the SM group and the PAS group. The INH group showed no significant changes. Excluding the hypoergic cases, the PAS group still showed a significant increase at one and two month periods and the SM group showed a significant decrease at the 8th month period. No change is again noted in the INH group.

Not tabulated, but also found by similar analysis of the data:

Far advanced cases show a significant increase in reaction at the first month of treatment; no significant change occurs in moderately advanced, minimal, or if hypoergic cases are excluded. White patients show a significant decrease at four and eight months if hypoergic cases are excluded. Negro patients demonstrate significant increases at one and two months for their entire group and also if hypoergic cases are excluded.

Patients under 50 years of age have a significant increase at one and two months of treatment. No changes are present if hypoergic cases are excluded or in patients over 50 years of age. Those with resolution of their disease have a significant increase at one and two months; excluding hypoergic cases a decrease is noted at 12 months. No significant change occurs in non-resolving patients. Those who convert their sputum to negative show a significant decrease in reaction at 12 months.

TABLE IV

CHANGES IN SIZE OF TUBERCULIN REACTION (in mm.) 1ST STRENGTH PPD UNDER CHEMOTHERAPY BY TYPE OF CHEMOTHERAPY AND DURATION OF TREATMENT—EXCLUDING HYPOERGIC CASES

TYPES OF CHEMOTHERAPY (Excluding Hypoergic Cases)										
	SM & PAS					SM & INH				
Mos. of chemo.	1	2	4	8	12	1	2	4	8	12
Mean of differences	+ 2.50	+ 1.88	+ .25	— 1.67	— .27	— .67	— 1.83	— 4.60	— 2.50	— 4.75
S.D. ±	3.81	3.74	4.27	2.85	4.90	4.32	3.48	4.50	4.76	3.06
t	2.63	1.90	.24	2.26	.21	.38	1.42	2.28	1.05	2.46
P	<0.05 >0.01	<0.1 >0.05	>0.1	<0.05 >0.01	>0.1	>0.1	>0.1	<0.1 >0.05	>0.1	<0.1 >0.05

Discussion

For many years studies have been made of tuberculin testing in treated and untreated cases of pulmonary tuberculosis. There is a natural and considerable variability in the tuberculin reaction in all patients, treated or untreated. No attempt will be made to list all the numerous reports. One of the early studies was made by Hayes[2] and co-workers. This study, made in pre-chemotherapy days illustrates this variability. They point out the well known fact that patients with an unfavorable course have a depression in their reactivity, but also patients who show improvement may show a depression in the reactivity during the course of treatment. The patients who were originally anergic usually showed an increase in reaction as their condition improved.

Studies of the tuberculin reaction following chemotherapy can be divided into three groups. One group, illustrated by Hirsch,[3] finds a decrease in reaction a month after chemotherapy. This appeared particularly to be

TABLE V

CHANGES IN SIZE OF TUBERCULIN REACTION BY MONTHS OF CHEMOTHERAPY FOR SM, INH OR PAS GROUPS FOR (A) ALL CASES AND (B) EXCLUDING HYPOERGIC REACTORS

ALL CASES														
	SM					INH					PAS			
Mos. of chemo.	1	2	4	8	12	1	2	4	8	12	1	2	4	8
Mean of differences	+ 2.79	+ 2.93	+ 1.61	+ .50	— .75	+ 1.64	+ 2.50	+ 2.23	+ 1.44	— 1.58	+ 3.16	+ 2.83	+ 2.06	+ .83
S.D. ±	4.92	4.99	6.92	6.36	5.24	5.12	5.74	7.25	6.83	5.67	5.32	4.57	5.82	5.11
t	3.07	3.12	1.23	.39	.64	1.50	1.95	1.44	.88	.96	3.33	3.37	1.95	.90
P	<0.01	<0.01	>0.1	>0.1	>0.1	>0.1	>0.01	>0.1	>0.1	>0.1	<0.01	<0.01	>0.1	>0.1

TABLE IV (Cont'd)

CHANGES IN SIZE OF TUBERCULIN REACTION (in mm.) 1ST STRENGTH PPD UNDER CHEMOTHERAPY BY TYPE OF CHEMOTHERAPY AND DURATION OF TREATMENT—EXCLUDING HYPOERGIC CASES

INH & PAS					Mixed					Sub-Total				
1	2	4	8	12	1	2	4	8	12	1	2	4	8	12
+	+	+	+	—	—	—	—	—	—	+	+	—	—	—
1.40	1.70	.91	1.20	1.43	1.00	.14	3.57	2.29	5.20	.72	.90	.87	1.08	1.90
5.20	4.41	4.42	4.59	4.72	4.58	3.67	4.91	4.88	5.07	4.39	3.90	4.78	4.16	4.93
.84	1.23	.68	.83	.82	.58	.10	1.93	1.25	2.29	1.03	1.41	1.14	1.57	2.13
>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	<0.1 >0.05	>0.1	>0.1	>0.1	>0.1	<0.05 >0.01

present in the patients with caseopneumonic tuberculosis. INH, one of the drugs used, showed the same reaction. Bettega[4] found a similar decrease using PAS. The patients were followed, however, only up to three months. Hewell[5] and co-workers, using INH, also found a decrease in the reaction emerging after one to two months with an increase again at the six month level. The second group of studies shows an increase in size of reaction at one to two months after starting treatment. This is illustrated by studies with INH. Pancotto[6] found an increase in reactions after INH in patients who improved while those who did not show increase had less favorable prognosis. This paralleled his previous studies using PAS and SM. Spada[7] also showed this increase in reaction to INH at two months.

Some investigators have found no significant change in the reaction during chemotherapy. Criep[8] and co-workers who used INH found no significant change at four weeks. Barnwell[9] and co-workers also found no change with SM. Korb[10] has tried to analyze reasons for all these dis-

TABLE V (Cont'd)

CHANGES IN SIZE OF TUBERCULIN REACTION BY MONTHS OF CHEMOTHERAPY FOR SM, INH OR PAS GROUPS FOR (A) ALL CASES AND (B) EXCLUDING HYPOERGIC REACTORS

EXCLUDING HYPOERGIC CASES

PAS			SM			INH					PAS				
12	1	2	4	8	12	1	2	4	8	12	1	12	4	8	12
+	+	+	—	—	—	+	+	—	+	—	+	+	+	—	—
.08	1.64	.86	.90	1.84	1.21	.63	.50	.81	.14	2.64	2.08	1.85	.52	.52	.64
5.40	3.74	3.95	4.73	3.24	4.76	4.87	5.05	5.04	4.87	4.54	4.07	3.77	4.27	3.91	4.77
.07	2.05	1.02	.87	2.50	1.11	.52	.40	.65	.11	1.89	2.59	2.50	.64	.67	.63
>0.1	>0.1	>0.1	>0.1	<0.05 >0.01	>0.1	>0.1	>0.1	>0.1	>0.1	>0.1	<0.05 >0.01	<0.05 >0.1	>0.1	>0.1	>0.1

crepancies and differences. He believes that discrepancies are due to differences in methods and material. There are differences in the length of time of the studies; the methods of testing; that is whether using one strength tuberculin and measuring diameters of induration or using serial dilutions; using PPD or old tuberculin; whether the area of edema or erythema is included; difference in type of patients, whether the cases are far advanced, moderately advanced or minimal; whether they show significant pulmonary disease or only positive tuberculin reactions; whether the study is done on animals or man; in the types of drugs used; whether the disease is pulmonary or extrapulmonary, and whether the cases are separated into the anergic, hyperergic or hypoergic groups.

Serial tuberculin studies of our patients followed for up to a year of chemotherapy show a distinct and highly significant increase in tuberculin allergy as compared to the reaction existing before treatment. This increase appeared as early as the 1st month and was still present at the 2nd month testing. The tuberculin reaction then steadily decreased, reaching baseline readings about the 8th month of treatment and at 12 months was below initial readings. Analyzing the groups according to chemotherapy, the SM-PAS group showed the same significant increase at one and two month readings. The changes in the SM-INH and the INH-PAS group parallel the changes shown in the SM-PAS group but were not large enough to be considered statistically significant.

Accumulating the cases into those receiving SM in combination, PAS in combination, or INH in combination, the SM groups and the PAS show the same initial increase in reactions. Since both these groups contain INH patients it is probable that larger numbers of the INH group would show the same increase, but this cannot be confirmed from the present study.

Nine of the 49 cases were considered as hypoergic; that is, they were considered as negative to the 1st strength PPD used in this study (showing an area of induration less than five millimeters). Significant increases in reaction were present throughout the first eight months of treatment, highly significant increases being present by the 2nd and 4th month.

When this group of hypoergic cases is separated from the remainder there now appears a depression in the reaction level of the remaining patients at eight months which falls below the base line at 12 months to a significant degree.

The early increase in reaction is again found, analyzing patients separately, to be particularly prominent in Negro patients; the younger group of patients, that is those under 50 years of age; and in the far advanced type of disease. Since the hypoergic group predominantly consists of white patients, this increase in reaction in Negro patients is doubly significant. The increase in reaction is associated with resolution of disease and occurs at about the same time. The group of resolving patients shows marked depression at the 12 month level. Whether a patient converts or not seems to make no difference as far as the increase in reaction in the early month is concerned since both groups show this increase.

Does serial tuberculin testing have a place in the control of patients

receiving chemotherapy? To a certain extent this depends on the question of the relation of allergy and immunity; that is, do changes in levels of allergy indicate change in the levels in acquired or natural immunity? The entire subject is still open to argument. Immunity and hypersensitivity can be disassociated, for it is known that hyperreaction alone does not prevent spread of disease. It is probable also that the tuberculin reaction lasts only as long as the body harbors viable tubercle bacilli. Overwhelming infection can also depress allergy. Is it due to a failure of cutaneous reactivity or due to a large excess of antigen?

Turner[11] believes that the study of the tuberculin reaction during the patient's lifetime is a valuable index of the patient's progress and may often indicate impending changes in the patient's condition under treatment. He considers the tuberculin reaction an index of the antibody-antigen ratio of the patient. A depressed reaction indicates an antigen level in excess of the antibody production with little antibody left to escape for testing. Hyperreaction indicates a high antigen stimulation with the release of excess antigen for systemic absorption. After treatment both the unfavorable hyperreactor and hyporeactor reach normal levels and changes thereafter might indicate impending relapse.

It is of interest that only two of our patients at 12 months of treatment showed a depression of the tuberculin reaction testing, that is reaction of less than five millimeters. Of course, they might have been positive to intermediate or 2nd strength testing. The reversal of the tuberculin test to negative has been recently reported in human infants in four cases by Robinson[12] and co-workers. These cases had only a positive tuberculin and no pulmonary lesion. Infants with pulmonary lesions did not show reversal of the tuberculin reaction under INH. It is not to be expected that patients in our group who were predominantly cavitary cases, with far advanced or moderately advanced disease, would show any completely negative tuberculin reaction, though the group as a whole did show a depression of reaction at the 12 month level. Undoubtedly they all still have living tubercle bacilli. It would be of interest to follow patients with only minimal disease who have long term chemotherapy on outpatient basis to see if they have further depression in the tuberculin reaction or whether any of them become negative.

Some concern has been expressed that the increase in tuberculin reaction initially under chemotherapy might have adverse local effects and the terminal depression in tuberculin reaction might depress the natural or acquired resistance. Since these questions are at present mainly hypothetical, no answer can be given at this time.

SUMMARY

Forty-nine adult males were tuberculin tested at intervals during chemotherapy for pulmonary tuberculosis up to one year of treatment. Patients were predominantly cavity cases with far advanced and moderately advanced disease. A significant increase in size of reaction was present at one to two months of testing. This increase occurred predominantly in Negro patients, those under 50 years of age, in the far advanced group

of patients and coincided with the period of resolution of the disease process.

To a certain extent, this increase in reaction was due to the presence of nine hypoergic cases who showed marked increases in reaction after starting treatment. When this group of patients is excluded, a depression in tuberculin reaction appeared at the 8th and 12th month treatment. This depression was not present in patients who did not convert their sputum. No significant difference in response of the tuberculin reaction under chemotherapy could be determined between different chemotherapy regimens. The significant increase at one to two month levels was present in both SM and PAS treated patients. Since both these drugs were used in combination with INH as well as with each other, it is possible that the INH patients would also show similar significant changes if a larger group of patients were used.

Though the role of specific allergy and its changing levels in patients treated with chemotherapy for pulmonary tuberculosis is still controversial, it is felt that further studies of the allergic state in such patients should prove to be of value and might produce further elucidation of problems of the patient's cellular and humoral response to his disease under treatment.

RESUMEN

Durante el tratamiento de tuberculosis hasta de un año, cuarenta y nueve hombres adultos fueron sujetos a reacciones de tuberculina a intervalos. Fueron enfermos predominantemente con excavaciones y con enfermedad moderada o muy avanzada. Se observó un aumento significativo del tamaño de la reacción al primero o segundo mes de tratamiento. Este aumento se vió especialmente en los enfermos negros, en los menores de 50 años, en el grupo de muy avanzados y concidiócon el período de resolución del proceso.

Hasta cierto punto, este aumento de la reacción se debió a la presencia de nueve casos hipoérgicos que mostraron marcados aumentos después de empezar el tratamiento.

Excluyendo este grupo de enfermos, una depresión de la reacción tuberculínica apareció del 8° al 12° mes del tratamiento. Esta depresión no se observó en los enfermos que no negativaron su esputo. No se encontró diferencia importante en la respuesta a la reacción tuberculínica bajo regímenes de quimioterapia diferentes. El aumento de las reacciones tuberculínicas al 1° o 2° mes se encontró tanto en los regímenes de PAS como en los Estreptomicina. Puésto que ambas drogas se usaron en combinación con INH así como entre sí, es posible que los enfermos tratados con INH muestren cambios similares si se observan en número suficiente.

Aunque todavía se discute el papel de la alergia específica en los enfermos tratados con quimioterapia de la tuberculosis, se cree que estudios ulteriores del estado alérgico en tales enfermos mostraría ser de valor y podría aclarar algo más el problema de la respuesta celular y humoral de los enfermos tratados.

RESUME

Chez 49 adultes du sexe masculin, on a recherché les réactions tuberculiniques à plusieurs reprises au cours du traitement chimiothérapique pour tuberculose pulmonaire, qui fut prolongé jusqu'à une année. Les malades étaient pour la plupart atteints d'une forme cavitaire avancée ou modérément avancée. On assista à un accroissement incontestable des réactions tuberculiniques pendant le premier et le deuxième mois du contrôle. Cette augmentation fut surtout nette chez les Noirs, chez les malades âgés de moins de 50 ans, et dans le groupe de malades sérieusement atteints. Elle coïncida avec la période de régression de l'atteinte.

Pour une certaine part, l'augmentation de la réaction s'explique par l'existence de neuf malades hypoallergiques chez qui les réactions augmentèrent notablement après la mise en route du traitement. Mis à part ce groupe de malades, une diminution de la réaction tuberculinique apparut au huitième et au douzième mois du traitement. Cette diminution ne fut pas notée chez les malades dont l'expectoration n'était pas devenue négative. On ne put mettre en évidence une variation des réactions tuberculiniques au cours de la chimiothérapie en fonction des différentes modalités de traitement. L'augmentation nette au niveau des premiers et deuxièmes mois fut notée aussi bien chez les malades traités par la streptomycine que chez ceux traités par le P.A.S. Depuis que ces deux médications sont utilisées en association avec l'isoniazide, aussi bien qu'associées entre elles, il est possible que les malades traités par l'isoniazide donneraient les mêmes résultats si l'expérience pouvait être conduite sur un groupe plus étendu de malades.

Le rôle de l'allergie spécifique et ses variations chez les tuberculeux pulmonaires traités par chimiothérapie est encore controversé. L'auteur pense que des études ultérieures sur l'état allergique de ces malades devrait donner des résultats valables et permettre d'élucider le problème de la réponse cellulaire et humorale de leur organisme sous l'influence du traitement.

ZUSAMMENFASSUNG

Es wurden 49 erwachsene Männer in Abständen mit Tuberkulin geprüft im Verlauf einer Chemo-Therapie wegen Lungentuberkulose bei bis zu einjähriger Behandlungsdauer. Bei den Kranken handelte es sich vorwiegend um cavernöse Fälle mit weit fortgeschrittener unr mässig weit fortgeschrittener Erkrankung. Eine beträchtliche Zunahme in der Grösse der Reaktion lag nach 1-2 Monaten Prüfung vor. Diese Zunahme ereignete sich vorwiegend bei Negern, bei Patienten unter 50 Jahren, in der weit fortgeschrittenen Patientengruppe und im Zusammentreffen mit der Periode der Rückbildung des Krankheitsprozesses.

In gewissem Grad war diese Zunahme der Reaktion der Ausdruck des Vorliegens von 9 hypoergischen Fällen, die ausgesprochene Zunahmen in der Reaktion aufwiesen nach Behandlungsbeginn. Wurde diese Patientengruppe ausgeschlossen, erschien eine Verminderung der Tuberkulin-Reaktion im 8. und 12. Behandlungsmonat. Diese Verminderung kam nicht vor bei Kranken, deren Sputum nicht negativ wurde. Ein erheblicher

Unterschied im Ausfall der Tuberkulin-Reaktion während der Chemo-Therapie zwischen verschiedenen chemotherapeutischen Methoden konnte nicht festgestellt werden. Die erhebliche Zunahme im Zeitraum von 1-2 Monaten kam bowohl bei mit Streptomycin als auch mit PAS behandelten Kranken vor. Da diese beiden Mittel ebenso in Kombination mit INH wie mit einander gebraucht wurden, ist es möglich, dass die INH-Patienten auch ähnliche erhebliche Veränderungen zeigen können, wenn man eine grössere Gruppe von Patienten beobachten kann.

Obwohl die Rolle der spezifischen Allergie und ihre wechselnden Grade bei Kranken, die eine Chemo-Therapie erfahren wegen Lungentuberkulose, noch umstritten ist, besteht die Möglichkeit, dass weitere Untersuchungen der Allergielage bei solchen Patienten sich als wertvoll erweisen und weitere Aufklärung geben würden über die Probleme der zellulären und humoralen Reaktion der Patienten auf ihre Krankheit im Verlauf der Behandlung.

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Closure of the Bronchial Stump Following Pneumonectomy

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Rienhoff,[12] Sweet[17] and Overholt,[9] have extensively written on closure of the bronchus—the vital point in pulmonary resection. Any method of bronchial closure, to be successful, must be based upon anatomical, physiopathological and technical details and considerations.

The fundamental principles of healing of the bronchial section should always be present with the least possible trauma (such as crushing of tissue), accurate approximation of the surfaces which are expected to heal together, adequate blood supply to the tissue involved, the necessity of an air-tight closure and, finally, the edges of the cut end of the bronchus should not be joined under tension at any point.

Many of the papers published on bronchial closure offer methods more or less effective,[3, 4, 10, 12] but without taking into account that the most frequent indications for pneumonectomy are cancer and tuberculosis. Regarding the former, Rabin[11] and coworkers prove or lead us to suspect the possibility of proximal metastasis in the submucosal lymphatics; and Griess[6] et al likewise mention the tendency of carcinomas to extend proximally along the bronchial wall. The foregoing, aside from the possible location of the tumor near the carina, makes it imperative that in the operation of cancer of the lung no other method for bronchial closure should be applied than that which is carried out after sectioning the main bronchus close to its origin. For bronchial closure in tuberculosis, it is a known fact that bronchial lesions diminish or subside from the distal to the proximal segment of the bronchus, and that the nearer to the trachea the section is done, the fewer lesions will be found on the bronchial wall.

The harmful effects on the suture of the increased intratracheal pressure which is brought about by coughing and straining, should also be considered in relation to the level at which the bronchus is sectioned and closed. It may be stated with Engineer Manuel Vera[19] that the section and suture of the bronchus close to its origin holds slight advantages in a mechanical sense over such methods where there remains an appreciable cul de sac, in which sedimentation takes place.[16]

Anatomical details are of utmost importance in obtaining good closure and healing when the bronchus is sectioned near its origin. Observation of the lower segment of the trachea and main bronchi (Figure 1C) show in many specimens the bronchial cartilage tends to project itself over the posterior aspect of the trachea in its distal segment, and clearly upon the posterior aspect of the main bronchi, both right and left, in such wise that if we section the main bronchi at 1 mm. or 2 mm. from their origin,

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that is to say over the first bronchial cartilage or at the space which separates the first from the second, we may observe that on the lower part the membranous and cartilaginous portions form a right angle. On the upper part the cartilage makes a curve which brings together the cartilage and membrane in an obtuse angle (Figure 1E[a]). In other specimens, on the other hand, the form agrees exactly with that reproduced in the majority of articles, that is, that the cartilaginous part of the wall is much more extensive than the membranous, but that when the bronchial section is made for an open closure the cartilaginous and membranous portions form

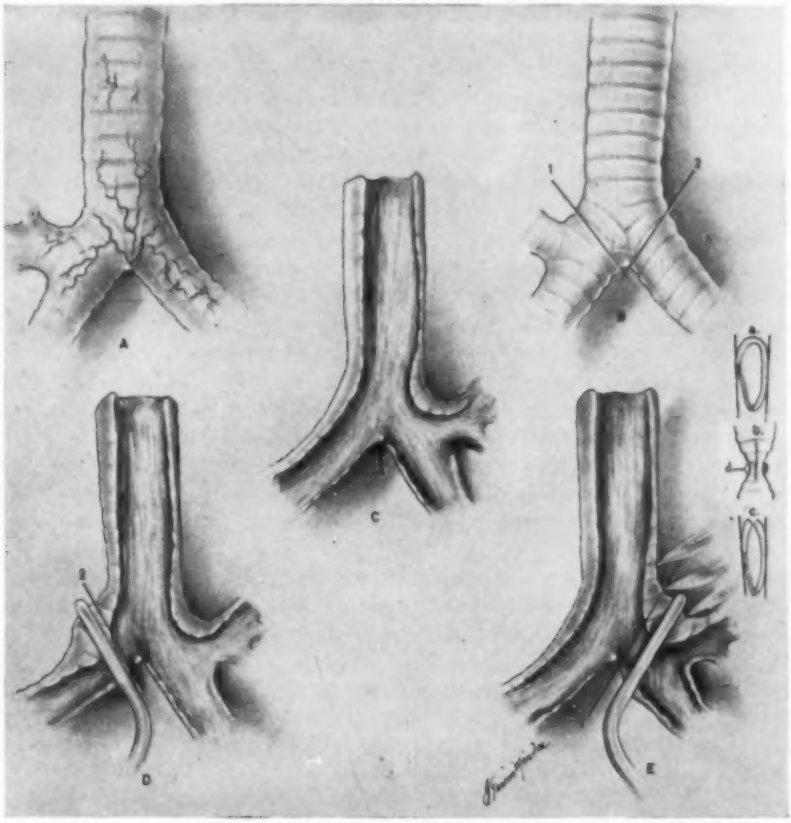

FIGURE 1: A) Vascularization of the anterior and inferior segment of the trachea. B) Lines one and two show the level where we section the main bronchi. C) In this figure may be clearly appreciated the extension of the cartilages over the posterior aspect of the inferior part of the trachea and of the main bronchi. Likewise may be appreciated the cartilaginous carinal nodule. D) The clamp has been placed on the left bronchus, care having been taken that the anterior and posterior walls be perfectly approximated in the inferior part. E) The clamp has been applied to the right bronchus and marks well the place of greatest prominence of the cartilaginous portion (a), which has to be sectioned including one or two tracheal cartilages and the first and second bronchial ones (b), section being left as shown in (c). The (d) marks the branches of the clamp which approximates the bronchial walls.

a right angle at both ends, the membranous part being almost the diameter of a semicircumference. This lack of proportions between the cartilaginous and the membranous portions creates a tension problem when the distal clamp and the sutures are placed, which on approximating the edges will produce a bending in the cartilaginous portion or a forced stretching of the membranous part. The result being an arched stump where the tension of the sutures on the bronchial walls is considerable.

At the carina there is sometimes a cartilaginous nodule (Figure 1C[3]) which frequently extends for several millimeters over the posterior aspect of the main bronchi. We shall later refer to the surgical importance of this anatomical detail.

Section of the bronchus close to its origin preserves an adequate blood supply to the cut ends, as it depends on the tracheal vessels themselves. One of the tracheal patterns of vascularization on its lower segment is presented under Figure 1A, something different from those described by Hovelacque[8] et al.

Technique of section and bronchial closure in pneumonectomy.—Once the main bronchus has been isolated (in the right side may be dissected as a first step and on the left side after the ligature and section of the pulmonary artery) we place a bronchial clamp approximately 1 cm. distal of its origin, being careful on applying the clamp that in the lower part the anterior cartilaginous and posterior membranous walls be in perfect apposition. There remains therefore in the upper part, much in evidence, the excess of cartilaginous tissue (Figure 1E[a]) which has to be sectioned at its most prominent point (Figure 1E[c]) so that both surfaces are perfectly bound together without tension. This section includes not only the bronchial cartilages but also one or two tracheal cartilages (Figure 1E). Care must be exercised not to touch the mucouse; hence we usually do not make a deep section of the wall and complete the fracture of the cartilages by means of pressure between the index finger and thumb until we are perfectly sure that the rupture of the cartilages has occurred, *elasticity having been completely overcome.*

Next, pulling on the clamp we inspect the origin of the contralateral bronchus, being careful with the vascularization of the trachea.

The bronchus is isolated by means of moist pads and the bronchial section begins by following a line which runs approximately over the first bronchial cartilage or contiguously outside of it (Figure 1B[1-2]).

As soon as a segment of the bronchus is cut any bronchial secretion present is aspirated, and the first stitch of a running suture[1] (chromic catgut No. 0 on an atraumatic needle) is passed and sectioning of the bronchus continues followed by the running suture until an air-tight closure is completed. If any bronchial blood vessel had not been previously tied, it is secured by forceps and separately tied.

In our opinion the running suture not only allows an airtight closure of the bronchial section but also has the advantage of permitting reinforcement of the suture by means of wire. This, placed as interrupted distal sutures proximal to the continuous one, can not cut into the bronchial wall.

At times there appears a cartilaginous nodule at the carina (Figure 1C[3]) which extends for a few millimeters over the posterior aspect of the main bronchi. In order to be able to conveniently tie the last stitch of the running suture it is necessary to section the nodule in the same manner as the upper part over the cartilage, so that at no time shall there be tension on the suture.

Immediately afterwards, to reinforce this suture, stitches with braided surgaloy No. 000 are passed proximal to it, mounted on a fine needle, so that no appreciable openings remain on the membranous portion of the bronchial wall. Usually four or five interrupted metallic sutures are necessary which are tied in a knot preferably over the posterior face, cutting the ends close to the knot so they may not offer risk to the nearby anatomical structures. In this respect when the bronchus is sectioned close to its origin the stump is never in contact with the right or left pulmonary arteries.

In the cases of pneumonectomy for tuberculosis where bronchial lesions are often extensive, we use the same method of sectioning and closure.

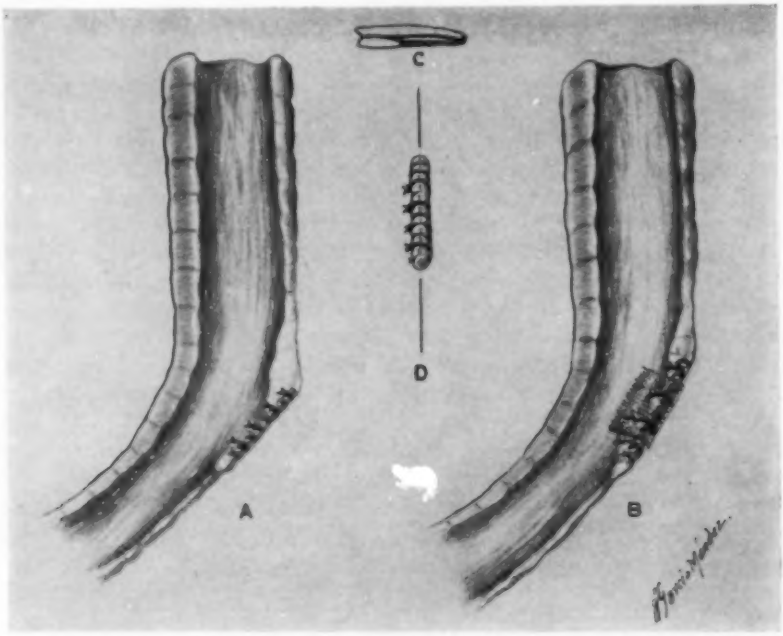

FIGURE 2: A) The right bronchus has been sectioned close to its origin and the stump has been closed by means of a continuous suture of chromic catgut No. 0, reinforced by four interrupted sutures of surgaloy No. 000. The left bronchus and the trachea now form one sole conduct. B) Whenever the bronchus presents considerable caliber or the section extends over the tracheal wall, we reinforce the suture previously marked in Figure (A) with a surgaloy mesh plate which perfectly fits the suture by means of two or three interrupted sutures of the same material. C) In this figure the necessity of sectioning the cartilaginous part in the most prominent location is made evident, so that the anterior and posterior surfaces may easily come together. D) Note that the stump once it has been sutured remains without any curvature whatever, which shows that there is no tension on the suture.

Care is taken to aspirate the contralateral bronchus through the open section. After the running suture has been passed, the edges of the bronchial section are cauterized with 10 per cent silver nitrate before proceeding with the wire sutures. We also resect any lymph node[15] suspicious of containing caseous material that may remain near to the bronchial stump. Ten days later we requested our bronchoscopist[14] to perform an endobronchial cauterization followed by a second, 10 days thereafter.

We believe that no case of bronchial fistula in 75 consecutive pneumonectomies, of which 35 were performed for extensive tuberculous lesions, may have been due in part to the cauterizations with silver nitrate.

Bronchial closure in special cases.—Frequently pneumonectomy is done for pulmonary cancer on patients over 60 years of age. Pulmonary emphysema is often encountered and the main bronchi are particularly dilated, which gives rise to a section surface of considerable extension.

This also occurs in some cases we have classified under megabronchi, in which extension of the sectioned surface is remarkable. In these cases the simple closure of the bronchus by the usual methods frequently gives rise to a dehiscence more or less extensive of the bronchial stump.

In the bronchial closure of these patients, we first use a continuous or running suture with chromic catgut No. 0 to the middle of the section, at which point we interrupt it and continue with a new running suture to the lower extreme. Then the first two stitches of the surgaloy are placed near the ends and in the center is placed a small plate of surgaloy mesh which is adjusted perfectly to the bronchial stump by means of two or three stitches of braided wire No. 000 of the same material (Figure 2B). This metallic plate is useful in preventing bronchial fistula in these cases.

In these cases it is necessary to be on the alert during the post-operative period as regards the level which the intra-pleural liquid reaches. For 20 days the liquid level is maintained below the aortic arch, by aspirations of the sero-hematic content. This is replaced by air in the necessary amount to maintain the mediastinum in the mid-line or slightly inclined towards the operated side. Each aspiration of liquid and consecutive substitution by air is followed by an injection of 500,000 units of penicillin and 1 gram of streptomycin in 10 cc. diluent.

Covering of the bronchial stump.—This principle which was thought at the time could be dispensed with, since antibiotics would prevent infection, which would in the end be the cause of the opening of the bronchial stump, is of the utmost importance. Our observations and those of many other authors, particularly Rienhoff,[12] Sweet[17] and Overholt,[9] prove that to cover the bronchial stump with viable tissue is of paramount importance in healing.

Many anatomical structures have been suggested for covering a bronchial stump in accordance with the type of incision the surgeon may use and the extension of the operation.[5, 18]

The anterior and posterior pleural flaps of the pulmonary pedicles have without doubt been used most (Rienhoff,[12, 13] Sweet,[17] Barata,[2] etc.) ; some authors have suggested parietal pleural flaps (Overholt[9]), pericardial flaps

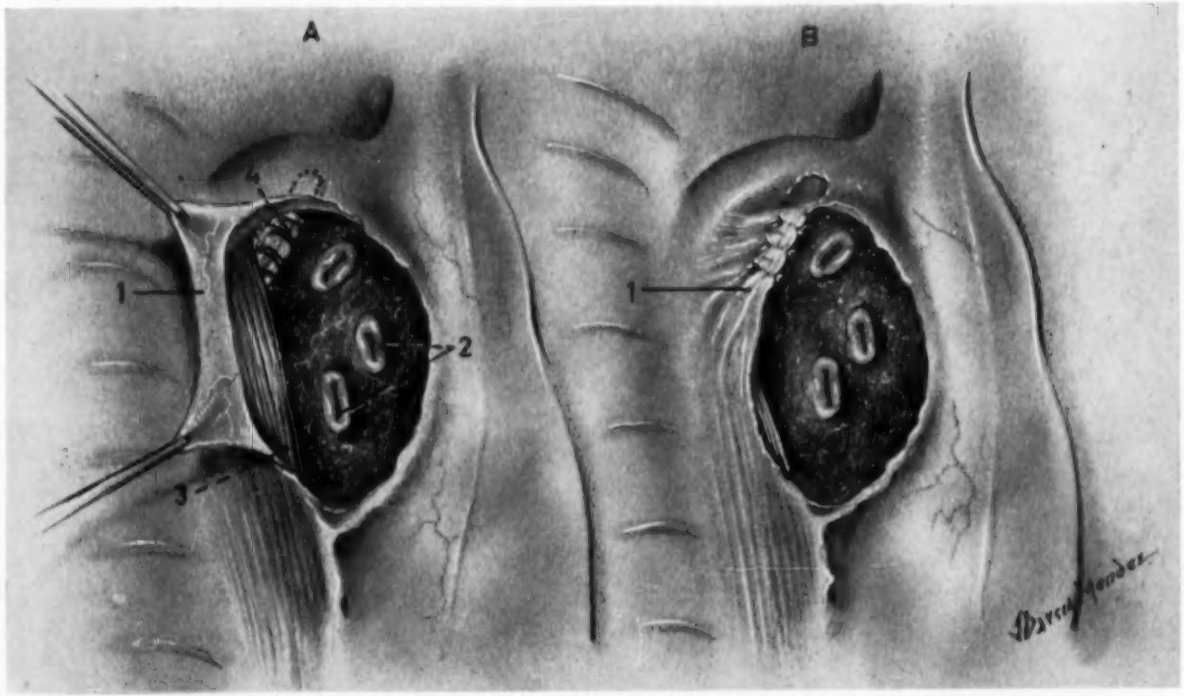

FIGURE 3: A) After the resection of the right lung has been made and the suture of the bronchial stump carried out, the latter remains in part under the arch of the azygos vein and against the esophageal wall. B) The bronchial stump has been buried making use of the posterior pleural flap of the pedicle, in accordance with Sweet's tehnique.

(Higginson[7]), pericardial fat grafts (Brewer[4]), intercostal muscles, etc.

Experience has taught us that by using lateral and face-down positions, pleuralization or covering of the bronchial stump is accomplished principally in right side pneumonectomy at the expense of the posterior pleural flap of the pedicle. The stump is buried in accordance with Sweet's[17] technique being careful not to injure the esophageal wall or the azygos vein (Figure 3A[1], B[1]). On the left side, frequently the bronchial stump, practically formed by a suture of the tracheal wall, enters deeply into the mediastinum and rests against the aorta, the periaortic tissue serving as an excellent means to cover said stump. On other occasions we use cellular fibrous tissue which in the form of a lamina accompanies the vagus nerve, covering the stump in the manner already described (Figure 4A[1], B[1]).

Whenever we use this type of bronchial covering we section the vagus nerve below the left recurrent branch. A technical detail which should never be omitted is that a sutured bronchial stump should always be in

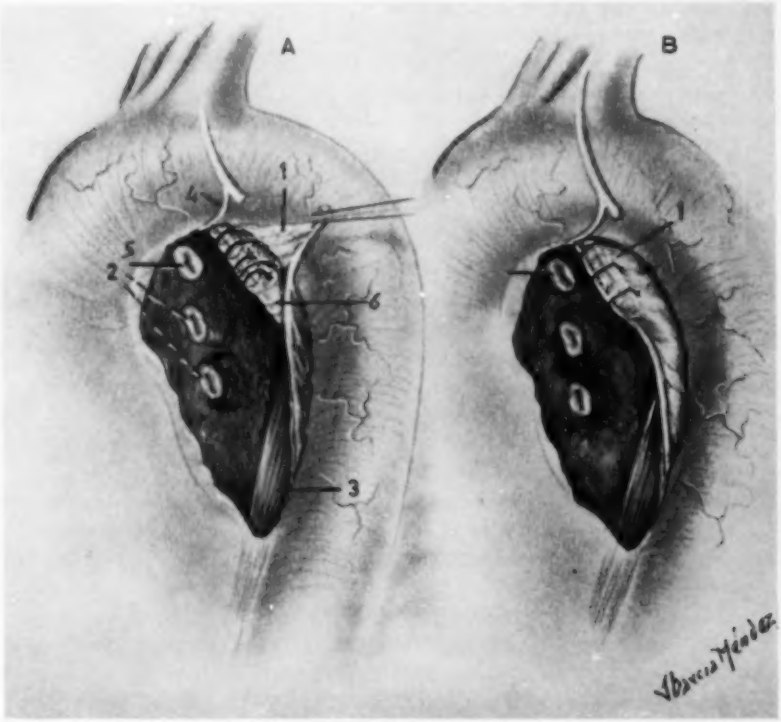

FIGURE 4: A) The left lung has been removed and the bronchial stump has been closed as has already been described. Covering of the stump is carried out by using the cellulo-fibrous layer which accompanies the vagus nerve. The vagus nerve has been sectioned below the outlet of the recurrent laryngeal nerve. B) The bronchial stump covered. Note that the vagus nerve remains placed on the anterior wall of the bronchus and the suture entirely covered.

contact with the tissue which has been used to reinforce it, but never facing the line of suture of the pleural flaps or covered incompletely.

SUMMARY

Modifications in the technique for bronchial closure, performed in 75 consecutive cases of pneumonectomy are presented.

The method described is summarized as follows.

a) Section of the main bronchus as near to its origin as possible.
b) Section of the cartilaginous portion on the place selected to prevent tension on the sutures.
c) Closure of the bronchial stump by means of a running suture of chromic catgut No. 0, reinforced by braided surgaloy No. 000 distal interrupted sutures.
d) Covering or reinforcement of the bronchial stump with viable tissues.

RESUMEN

Se presentan modificaciones en la técnica de cierre del bronquio en 75 casos consecutivos de neumonectomía.

El método que se describe se resume así:

a) Sección del bronquio principal tan cerca como sea posible de su origen.
b) Sección de la porción cartilaginosa en el lugar escogido para evitar tensión ejercida sobre las suturas.
c) Cierre del muñón bronquial por una sutura contínua de catgut crómico No. 0 reforzando la sutura con surgaloy trenzado No. 000 distalmente, por puntos separados.
d) Cubrir o reforzar el muñón bronquial con tejidos viables.

RESUME

L'auteur présente une technique modifiée d'occlusion du moignon bronchique qu'il a utilisée dans 75 pneumonectomies successives.

La méthode décrite se résume de la façon suivante:

a) Section de la bronche principale aussi près que possible de son origine;
b) Section de la portion cartilagineuse à la place chonsie pour éviter la tension des sutures;
c) Fermeture du moignon bronchique par un surjet de catgut chrome N°0 avec un second plan à la soie N°000 par points séparés;
d) Des tissus viables doivent recouvrir ou renforcer le moignon bronchique.

ZUSAMMENFASSUNG

Es wird berichtet über Modifikationen in der Technik des Bronchialverschlusses, wie sie an 75 auf einander folgenden Fällen von Pneumonektomien vorgenommen wurden.

Die beschriebene Methode lässt sich wie folgt zusammenfassen:

a) Durchtrennung des Hauptbronchus, so nahe seinem Ursprung wie möglich.
b) Durchtrennung des knorpeligen Anteiles an der Stelle, die dafür bestimmt ist, den Zug der Nähte zu verhindern.

c) Verschluss des Bronchialstumpfes mittels einer fortlaufenden Naht mit Chrom-Catgut Nr. 0, verstärkt durch distal aussetzende geflochtene Nähte mit Surgaloy Nr. 000.

d) Bedeckung oder Verstärkung des Bronchialstumpfes mit lebensfähigem Gewebe.

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Surgery in Pulmonary Coccidioidomycosis

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A review of the current literature shows that the indications for surgery in pulmonary coccidioidomycosis remain unsettled at the present time. Goldstein and McDonald[5] feel that the mode of therapy in this disease parallels closely that of tuberculosis, usually without pneumothorax or surgical intervention. Lindskog[10] in his text, points out that unfortunately the late results of lobectomy for residual cavity have not been perfect, a number of cases have developed additional lesions in remaining lobes with persistent positive sputum. Cotton[3] reported only one death among 30 cases treated with pulmonary resection and that was from coronary occlusion. At last follow-up three of the 29 remaining had non-coccidioidal complications though none had evidence of reactivation of coccidioidal infection. Cogswell et al[2] felt the indications for resection in pulmonary coccidioidomycosis to be 1. spontaneous pneumothorax with unexpanding lung, 2. gross hemoptysis in presence of a persistent cavity, 3. solid tumor, possibly confused with carcinoma and, 4. large blocked or expanding cavity. They feel that post operative complications have to do with residual coccidioidomycosis in the bronchus draining the operated area. Hyde[8] notes a case with spontaneous healing of a recurrent coccidioidal cavity and mentions 17 cases of coccidioidomycosis followed for up to eight years without surgery that have remained well. He feels hemorrhage is the main indication for resection.

The indications for resection according to Guilfoil[7] are essentially the same as those mentioned above.

Trimble[18] feels that cavities should be surgically removed if they fail to close under medical management. He also believes that coccidioidomas or the coin-like lesions should be explored and removed. Bass[1] has voiced the opinion that surgery should be reserved for cases with severe recurrent hemoptysis or spontaneous pneumothorax with empyema. Willett and Weiss[20] conclude that surgical measures may be exceptional circumstances where such could be applied with benefit.

Melick[11] in 1950 reported the result of inquiries sent to the members of the American Association for Thoracic Surgery in which 224 physicians replied. In general surgeons felt that a persistent long standing granulomatous cavity is occasion for resection. In all, 98 cases of excisional therapy were reported. The indications were persistent cavitation, recurrent hemorrhage, productive cough, suspicion of neoplasm, granuloma, failure of the lung to expand following spontaneous pneumothorax, inability to make the diagnosis and residual cyst. In this article Dr. C. E. Smith of San Francisco is quoted: "As for the recurrence of cavities after thora-

From the Department of Surgery, Thoracic Surgical Service, U. S. Naval Hospital. The opinions expressed in this article are those of the writers alone and do not necessarily reflect the official attitude of the United States Navy Department.

cotomy and resection, in view of the apparent remoteness of that complication, it will require time to decide whether or not thoracoplasty should be performed soon after resection. One wonders if thoracoplasty might be reserved for the complications. My own position is that I do not believe in any intervention unless there are symptoms and specific reasons are present. Most cavities close if left alone, and most cavities which do not close are asymptomatic. If incapacitating symptoms are present, however, then I would certainly use thoracotomy if phrenic crush failed to cure the patient."

In this same article Dr. W. A. Winn of Springville, California said: "I am inclined to believe the surgeons are somewhat overdoing resection for this disease. Perhaps the indications for resection have to be more sharply defined. The existence of cavitation *per se* should not mean pulmonary resection, but under certain circumstances surgical removal does become necessary." Dr. Winn has since reported treating 30 cases of cavitary pulmonary coccidioidomycosis with collapse measures ranging from pneumo-

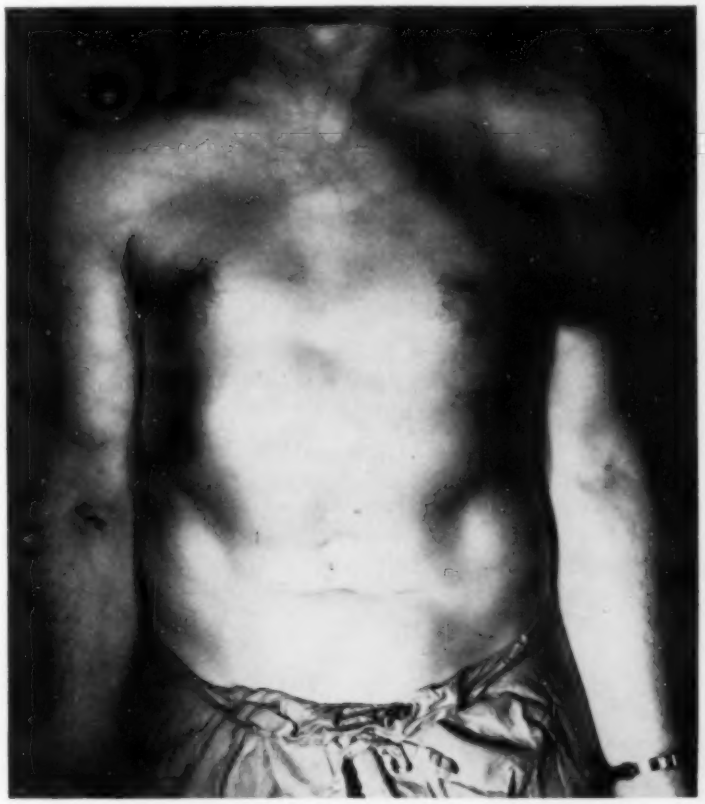

FIGURE 1: Infra red photograph of C. H. showing collateral venous circulation resulting from vena cava obstruction.

thorax with and without pneumonolysis to pneumoperitoneum with and without phrenic paralysis.[21] In 10 of the cases these measures were ineffective in stopping bleeding or preventing further increase in size of cavities.

Forsee[4] on the other hand, now feels that pulmonary coccidioidomycosis is a surgical disease.

Because of the differences in opinion expressed, the following cases of pulmonary coccidioidomycosis, treated at the U. S. Naval Hospital, St. Albans, N. Y. are presented to illustrate the results, including complications which may be obtained by excisional surgery.

Results

Seven cases of pulmonary coccidioidomycosis were treated surgically here from July 24, 1951 to May 31, 1955. In five of the seven the diagnosis was made by culturing the organism, C. immitis. In one the organism was seen on smear of the surgical specimen. In the remaining case the diagnosis was presumptive since the organism was not found. However, the skin test, complement fixation and precipitin tests were positive for coccidioidomycosis and the tuberculin skin test was negative.

In all seven cases the lesions were localized. In three they were cavitary and in four the lesions were solid. Indications for resection were clear: hemoptysis in two, coin lesions of unknown etiology in three and cavities of unknown etiology in two.

Only one case demonstrated an extrapulmonary lesion and this appeared six months after surgery. This patient (R. D.) developed vague central nervous system symptoms and C. immitis was grown from his cerebrospinal

Figure 2: Appearance of T. P. after complete recovery from surgery.—*Figure 3:* Photomicrograph of the lesion removed from T. P. (100 X).

TABLE I

Case	Age	Race	Sex	Lung Lesion	Other Lesions	Skin Tests	Compl. Fix.	C. Immitis Identified	Treatment		Complication and Follow-up
									Med.	Surg.	
C. H.	36	W	M	Coin lesion, R.U.L.	None	C—+ H—o P—o	Positive	No smear or culture	Streptomycin for 42 days. 1951	Right pneumonectomy 2/23/51. Right thoracoplasty 7/24/51	Developed superior vena cava obstruction by Dec. 1952. No further progression. Working 9/15/55
R. D.	29	W	M	Coin lesion, posterior segment, R.U.L.	C.S.F. Culture Positive 7/7/52	C—N H—N P—N	1-128 7/54	Culture of empyema pus pos.	2 HS 23 gms 1952 AS 1.65 gms. 1954	Lesion excised R.U.L. 1/22/52	Decortication and empyema drainage for unexpanded lung, 2/25/52. Developed chest wall draining sinuses along with unexpanded lung for which block resection done on 6/16/52. Underlying lung decorticated at same time. On duty USAF 10/26/54
B. L.	28	W	M	Coin lesion, L.U.L.	None	C—+ H—+ P—o	Negative	Section of lesion pos. No culture	None	Lesion excised L.U.L. 2/25/52	
M. W.	22	W	M	Cavity, R.U.L.	None	C—+ H—o P—+	Positive 1-2	Culture of excised lesion pos.	Bed rest only	Posterior seg. R.U.L. 5/29/52 resected	No complications. Well, 9/21/55
T. P.	21	W	M	Cavity, posterior segment, R.U.L.	None	C—+ H—o P—+	Positive 1-80	Culture of pleural peel and gastric washings positive	P.A.S. (? gms.) 2 HS 16 gms. 1953 AS 2.3 gms. 1953	Decortication, right lung. Posterior seg. R.U.L. resected, 10/20/52	Decortication for b.p.f. and empyema, 12/18/52. b.p.f. again developed for which a thoracoplasty done on right, 5/12/53. Well, 3/54
A. S.	39	N	M	Cavity, R.L.L.	None	C—+ H—o P—+	Positive	Culture of bronchial aspirate positive	AS 2.225 gms. 1954	Resection of superior segment, R.L.L. 10/7/54	None, well, 1/55
O. F.	20	W	M	Coin lesion, ant-segment, R.U.L.	None	C—+ H—o P—+	Negative	Culture of excised lesion, positive	None	Resection of lesion, R.U.L. 5/31/55	None, well, 8/55

Legend: C—Coccidioidin
H—Histoplasmin
P—PPD

\+ positive
o negative
N not done

2 HS—2 hydroxy-stilbamidine
AS—Amino-stilbamidine

fluid. He was then treated with hydroxy-stilbamidine, (1952) and amino-stilbamidine, 1954). As of October 1954 he was well and on duty with the U. S. Air Force, two and one-half years after the meningeal coccidioidal infection was discovered.

Two other patients received stilbamidine derivatives post operatively. One had streptomycin and one para-aminosalicylic acid.

The original operations were as follows: excision of local lesion, three; resection of superior segment, right lower lobe, one; resection posterior segment, right upper lobe, one; decortication and resection posterior segment, right upper lobe, one; and right pneumonectomy, (done at U. S. Naval Hospital, San Diego), and thoracoplasty, one.

There was no death and follow-up of five to 50 months post operatively revealed all to be well and working.

Post operative complications developed in three reported in more detail below. In a fourth case, (A. S.), post operative gastric lavage cultures were intermittently positive for C. immitis and remained so despite amino-stilbamidine therapy. However, he is clinically well, and since January 1955 cultures from gastric washings have been negative.

Case Reports

C. H. This 36 year old man was admitted to the U. S. Naval Hospital, San Diego, because of primary atypical pneumonia. X-ray film showed "disease" in the right lung and right hilum. Because of the possibility of bronchogenic carcinoma, right thoracotomy was done January 31, 1951. A stony hard posterior segment of the right upper lobe was found which on frozen section revealed non-specific inflammatory reaction. Lobectomy appeared technically impossible so the wound was closed and at a second operation, February 23, 1951, right pneumonectomy was done. Pathologic study revealed fibrocaseous granulomatous inflammation. No organism was seen. Skin tests revealed positive reaction to a 1-10 dilution of coccidioidin and no reaction to tuberculin. Complement fixation and precipitin tests were positive for coccidioidomycosis in low titer.

On May 31, 1951, he was transferred to the U. S. Naval Hospital, St. Albans where a tailoring thoracoplasty was done July 24, 1951. He was discharged without symptoms August 30, 1951.

He was readmitted December 9, 1952, because of symptoms of superior vena cava obstruction which gradually developed over the intervening time. His physical findings were corroborative, venous pressure in the arms was 38 cm. water and angiogram revealed obstruction of the superior vena cava in the mediastinum apparently secondary to inflammatory reaction in the mediastinal nodes. He was discharged December 19, 1952, and has working since with no apparent progression of his clinical picture.

Comment: Although this is not necessarily a direct surgical complication, this situation is one which obviates an otherwise satisfactory result.

R. D. This 29 year old white man had a routine chest x-ray film December 20, 1951, which revealed a small round localized lesion in the right upper lobe. He had no complaint at that time. There was no positive physical finding. On January 22, 1952, right thoracotomy was done at the Air Force Hospital, Dow Air Force Base, and the lesion was excised. The lung did not re-expand postoperatively and pleural infection developed. On February 23, 1952, the right empyema was drained and the right lung decorticated. Postoperatively the lung failed to expand and empyema again resulted.

He was transferred to the U. S. Naval Hospital, St. Albans, March 8, 1952 with persistent empyema. Six intercommunicating sinuses of the chest wall developed, following admission. On June 15, 1952, right thoracotomy with block excision of the infected tissues of the chest wall was done and the right lung was decorticated. Postoperatively there was slow expansion of the lung despite some low grade septic reaction early in the postoperative course. Review of the slides of the original lesion at this time revealed coccidioidal granuloma instead of tuberculosis as was the original impression. Cultures of the pus yielded pure growth of C. immitis. Sections of the pleural membrane removed at the decortication revealed coccidioidomycosis also. On July 7, 1951, he complained of headache and lumbar puncture was done. C. immitis grew out of the cerebrospinal fluid. The diagnosis was apparently disseminated coc-

cidioidomycosis with meningeal involvement. He was transferred to another hospital and given a total of 23 grams of 2-hydroxy-stilbamidine. Following this he was returned to St. Albans and after several months of observation at gradually increasing activity, he was discharged, April 7, 1952.

He was well until checked at another hospital in June, 1954 when he was told that he needed more treatment. He was therefore readmitted to U. S. Naval Hospital, St. Albans, June 15, 1954. Spinal fluid at that time showed elevated protein and positive Pandy reaction. He was given 1650 mgms. of amino-stilbamidine and tolerated it well, being discharged July 12, 1954. However, in December, 1955, he was readmitted to the hospital with disseminated coccidioidomycosis with meningeal involvement.

T. P. This 21 year old white man was admitted to the U. S. Naval Hospital, St. Albans, February 16, 1952. In August of 1950 he developed left spontaneous pneumothorax which cleared without treatment. A similar episode occurred in March, 1951, and also cleared without treatment. In August, 1951, he was found to have a cavity in the right lung on a reenlistment x-ray film and while being studied in the Fitzsimmons Army Hospital he had a third spontaneous pneumothorax. This also cleared but the cavity remained. His workup was extensive and though tuberculosis was seemingly ruled out, one of 18 sputum examinations was positive for acid fast bacilli.

At this point he was transferred to St. Albans, December 16, 1951. His workup revealed positive first strength tuberculin test and doubtful reactions to histoplasmin and coccidioidin. He had two episodes of spontaneous pneumothorax the last being on the right and necessitating closed thoracotomy. He had previously received pneumoperitoneum because the cavity appeared to have developed reaction around it, inferring activity. He was started on para-aminosalicylic acid and on October 20, 1952, decortication of the right lung with resection of the posterior segment of the right upper lobe was accomplished. Post operatively a broncho-pleural fistula developed with empyema. This resulted in marked pleural thickening and poor expansion of the remaining lung. On December 18, 1952, decortication of the right lung was again performed but persistent air leak and pocketed fluid were encountered postoperatively. At this point C. immitis was cultured from the empyema fluid and the original specimen was diagnosed as coccidioidomycosis. Repeat skin test with coccidioidin was positive and the complement fixation test was positive to a titer of 1:80. The empyema cavity persisted despite conservative therapy. On May 12, 1953, an eight rib tailoring thoracoplasty was done on the right. In two months the broncho-pleural fistula closed but cultures of pleural fluid done during this period were positive for C. immitis. On July 20, 1953, he was started on hydroxy-stilbamidine isothionate and he received a total dosage of 8 grams up to August 14, 1953. A second course of 8 grams was given ending on October 9, 1953. All laboratory studies were normal during this time but cultures remained positive for C. immitis. He was then given a total of 2.3 grams of 2-amino-stilbamidine from December 10, 1953, to December 21, 1953. Except for transient mild gastrointestinal upset and mild icterus which disappeared after treatment he tolerated this well. Following treatment seven gastric cultures were negative for C. immitis. His chest x-ray film findings had remained stable since the thoracoplasty of May 12, 1953. He was discharged in March 1954 without symptoms. Follow-up in the early spring of 1955 found him well and working.

Discussion

Pulmonary coccidioidomycosis has been generally found to be a benign, self limited disease. Only rarely does such a case disseminate or produce a progressive process. Man to man infection is unknown.

Pulmonary cavitation is apparently the commonest complication of pulmonary coccidioidal disease according to Cotton.[3] These cavities are benign as indicated by their persistence for years without difficulty for the patient as noted by Pittman and Kane[13] and Winn.[21] In addition, dissemination in cavitary disease seldom occurs.[15]

Most authors of experience are of the opinion that, except for persistence of C. immitis in sputum, the localized pulmonary form of coccidioidomycosis is a self limited disease which does not recur. Joress and Bushueff[9] reported three cases of apparent reactivation but they more likely are slowly progressive, rather than reactivated arrested cases, in the minds of the present authors.

Three in this series were treated with stilbamidine derivatives. Schoen-

bach and his group[14] were the first to report their effectiveness in blastomycosis. Since the effect of these drugs on other deep mycosis has been investigated. Snapper et al[16] reported *in vitro* effectiveness against H. capsulatum and Nejedly[12] presented a case of localized palatine histoplasmosis which cleared while under 2-hydroxy-stilbamidine therapy. Taschdjian[17] tested these drugs against S. Schenki, C. neoformans and N. asteroides. The growth of C. neoformans and S. Schenki was inhibited, that of the latter organism being most pronounced. Gordon et al[6] found no effect of the stilbamadine drugs on coccidioidomycosis in mice and observed *in vitro* inhibition of growth of C. immitis only at a concentration of 100 micrograms per milliliter. Whitehill and Rawson[19] treated a case of generalized cryptococcosis with 2-hydroxy-stilbamidine with apparent success, though follow-up was only for a few months.

Of the three cases in the present series receiving these drugs, only R. D. with meningeal involvement appears to have been significantly benefited. No conclusions seem warranted therefore from our experiences with stilbamidines.

Since the localized form of pulmonary coccidioidomycosis is generally self limited and since uncomplicated cavitary disease apparently causes no harm, resection appears to be indicated only in cases where coccidiodoma could be confused with carcinoma or in complications of coccidioidal cavitation. These, as listed by Cotton[3] are: 1. giant cavity with compression of healthy lung and shift of the mediastinum, 2. secondary infection of the cavity, 3. rupture of the cavity with empyema, self limited pneumothorax or open bronchopleural fistula, 4. non-expansile lung, and 5. hemoptysis.

Though the present series of cases is far too small to draw any definite conclusion, there is a suggestion that resectional surgery in coccidioidomycosis is more frequently complicated by postoperative persistent air leak and pleural disease than is similar surgery in other conditions. This tends to emphasize the need for clear indications for resection in coccidioidomycosis.

SUMMARY

1. Seven cases of pulmonary coccidioidomycosis were operated upon at the United States Naval Hospital, St. Albans, New York during a three year and 10 month period.

2. All are well but three developed serious postoperative complications.

RESUMEN

1. Siete casos de coccidioidomicosis pulmonar fueron operados en el Hospital Naval de los Estados Unidos en St. Albans, New York, durante tres años y diez meses.

2. Todos están bien, pero tres tuvieron complicaciones postoperatorias serias.

RESUME

1. Sept cas de coccidioidomycose pulmonaire furent opérés à l'Hôpital Naval des Etats-Unis à St-Albans, New-York, pendant une période de trois ans et dix mois.

2. Tous les opérés sont en bonne santé, sauf trois d'entre eux qui furent atteints de graves complications post-opératoires.

ZUSAMMENFASSUNG

1. Sieben Fälle von pulmonaler Coccidioidomycose wurden während eines Zeitraumes von 3 Jahren und 10 Monaten in dem US-Marine-Krankenhaus St. Alban in New York operativ behandelt.

2. Alle befinden sich wohl, aber in 3 Fällen entwickelten sich ernsthafte postoperative Komplikationen.

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Rupture of Papillary Muscles: Occurrence of Rupture of the Posterior Muscle in Posterior Myocardial Infarction

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Introduction

Rupture of a papillary muscle of the heart has been considered an unusual complication of myocardial infarction. Although first recognized as early as 1803, only 56 cases have been reported to date.

The literature was reviewed by Davison[1] in 1948. He added three cases to 26 previously reported. Other instances have been described by Glendy and White; Payne and Hardy; Askey;[2] Smith, Schwartz and Canelli; Hope and Askey;[3] Craddock and Mahe;[4] Briggs; Ritama and Heino;[5] Segall and Sharp;[6] Oeser;[7] and Reuter.[8]

Our main purpose in presenting five more cases is to emphasize the typical combination of rupture of the posterior papillary muscle following simultaneous infarction of that muscle and of the posterior wall of the left ventricle. We should also like to note that in our experience, rupture of a papillary muscle in general has not been too rare an occurrence. We saw the five cases reported here in a relatively short period of time, and we know of an additional five cases which were not included because of insufficient clinical data.

Case 1: E. P., a 78 year old man, entered the hospital on August 30, 1954, complaining of retrosternal pain radiating into both arms. The pain started the night before admission and had never been present before. He had been treated for bronchial asthma during the previous six months. Examination revealed a weak, lethargic, and drowsy man, who appeared younger than the stated age. The blood pressure was 100/70 mm. Hg., and the pulse was 60 per minute and regular. Scattered expiratory wheezes were heard. The heart was not enlarged. No thrills or murmurs were found. The electrocardiogram showed an acute posterior myocardial infarction. The sedimentation rate was slightly elevated. He was placed in an oxygen tent and started on dicumarol. He did well during the first 17 days of hospitalization and had only an occasional bout of pain. During the afternoon of the 18th hospital day he suddenly became dyspneic, cold, and sweaty. His pulse increased to 120 and his blood pressure was unobtainable. For the first time a moderately loud, medium-pitched, systolic murmur was heard at the apex with transmission to the axilla. No thrill was felt. The diagnosis of a ruptured papillary muscle was made at this time. He expired three hours later in circulatory collapse.

On autopsy the posterior papillary muscle showed a complete fresh rupture located 1.5 cm. below the cranial end. The upper portion of the muscle was firm and had a yellowish surface. In the vicinity of the tear the tissue was softer and grayish-

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Cases 1, 2 and 5 are from General Rose Memorial Hospital; Case 3 from Colorado General Hospital; and Case 4 from Porter Sanitarium and Hospital.

The latter case was reported previously with regard to pulmonary changes (E. F. Geever, Karl T. Neubuerger and E. K. Rutledge, Atypical pulmonary inflammatory reactions, *Dis. Chest*, 19:325, 1951).

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pink. The lower portion exhibited accentuated discoloration and softness. It showed sub-endocardial hemorrhage. The upper half of the posterior wall of the left ventricle had a mild aneurysmal bulge. The myocardium in this field showed decreased consistency and yellow to light tan discoloration. There was recent fibrinous hemorrhagic pericarditis over the posterior wall. Old fibrosis was found in the anterior wall. Coronary sclerosis was severe, and the right coronary contained an older thrombus which measured 6 cm. long. The lungs were edematous.

Case 2: E. K., a 61 year old man, was admitted to the hospital on December 12, 1954, with chest pain of 12 hours duration. He had apparently been in good health before this admission. He had been a heavy smoker most of his life and had suffered from chronic cough and some wheezing for several years. On examination the blood pressure was 134/82, and the pulse was 82 and regular. The heart sounds were distinct and a faint apical systolic murmur was heard. The lungs contained numerous wheezes bilaterally. The electrocardiogram showed acute posterior myocardial infarction. The white blood cell count was 12,600 per cu. mm. with 91 per cent polymorphonuclears. The sedimentation rate was moderately elevated. He was placed in an oxygen tent and immediately started on heparin and dicumarol. On the second hospital day the heart rate increased; the wheezing became worse and was associated with some dyspnea. Because of impending failure he was digitalized with some improvement. He did fairly well until the morning of the eighth hospital day when he suddenly became quite dyspneic and showed evidence of shock. His condition gradually deteriorated and he died eight hours later. During this time, his chest was so noisy due to wheezes, rhonchi, and moist rales that it was impossible to hear the heart sounds.

The moderately enlarged heart was flabby on autopsy. The epicardial surfaces, especially over the posterior wall of the left ventricle, were covered with shaggy masses of fibrin. There was a sight aneurysmal bulge of the posterior wall. The left posterior papillary muscle was ruptured. A 1.5 cm. gap separated the upper and lower portions which respectively measured 3 and 2 cm. in length. The muscle was soft and yellow-gray. The bulk of the posterior ventricular wall and a small adjacent portion of the septum were similar and mottled with bright yellow patches. Calcific sclerosis, with narrowing of all branches, was found in the coronaries. The right coronary had a near-total occlusion of a 12 mm. segment with constriction of the wall, intimal ulceration and presence of soft brownish thrombotic material. The lungs showed a moderate degree of edema.

Case 3: H. S., a 76 year old butcher, was admitted to the hospital on October 18, 1954, with chest pain of 24 hours duration. He had been treated for basal cell carcinoma of the lips in June, 1954, when an electrocardiogram was normal and no heart murmur was heard. Examination revealed a thin well developed man in acute pain. The blood pressure was 86/70 mm. Hg., and the pulse was 88. The heart was not enlarged. The heart sounds were distant. A low-pitched systolic murmur was heard in the aortic and apical regions with maximum intensity at the apex. No thrill was felt. The electrocardiogram showed an acute posterior myocardial infarction. The sedimentation rate was moderately elevated. The white blood cell count was 17,500 with 92 per cent polymorphonuclears.

He was immediately given oxygen, demerol, wyamine, heparin, and dicumarol. He did fairly well for two days but on the third hospital day his blood pressure began to fall in spite of intravenous wyamine. He rapidly went into deep shock and died on the morning of the fourth hospital day.

At autopsy the heart weighed 460 grams. The posterior wall of the left ventricle and the interventricular septum were yellow-red, mottled, softened and flabby. The base of the posterior papillary muscle was torn, ragged, and covered by an adherent blood clot. The proximal fragment of the muscle was entangled in the chordae tendineae. The left coronary artery was almost occluded by calcific plaques. The right coronary artery had numerous plaques and was occluded by a reddish-brown thrombus 4 cm. from its origin. The lungs exuded abundant foamy fluid from the cut surface.

Case 4: N. W., a 63 year old gardener, was admitted to the hospital on September 11, 1947, with severe substernal pain of 24 hours duration. There had been no previous attack of pain. Examination revealed an apprehensive man with moderately severe chest pain. The blood pressure was 156/100 and the pulse was 98 and regular. Respirations were 26 per minute. Medium and fine rales were heard in the upper lung field on both sides. The heart was slightly enlarged and no murmur was heard. The electrocardiogram showed inverted T-waves in Leads I and II and V6 suggesting a lateral infarction, probably recent but not acute. The white blood cell count was 13,350, with 84 per cent polymorphonuclears. The sedimentation rate was normal.

He was placed in oxygen and given aminophyllin and morphine. His chest pain decreased in a few days. An electrocardiogram on the fifth hospital day showed much less T-wave inversion. However, the patient developed a viral pneumonia which did not respond to antibiotic treatment. He declined steadily and on the 15th hospital

day suddenly became worse. His blood pressure fell to 100/70 and his pulse became rapid and irregular. A high-pitched systolic murmur of maximum intensity at the apex was noted for the first time. He expired two days later.

At autopsy the moderately enlarged heart showed several small areas of fibrosis and numerous patches of fresh necrosis in the lateral aspect close to the surface. The posterior papillary muscle was completely torn at its base. The latter was covered was a 4 cm. grayish-red thrombus with soft yellow center. The chordae tendineae were twisted, coiled, and entangled. The right coronary artery was essentially free of sclerosis. The left coronary artery showed thickening of the wall with calcification and large, coalescing, yellowish plaques which greatly narrowed the lumen. Thrombosis was not observed. The lungs showed the picture of atypical pneumonia.

Case 5: P. K., a 67 year old man, entered the hospital on September 15, 1953, complaining of intermittent substernal chest pain of one week's duration. Examination revealed a well-developed man in no apparent distress. The blood pressure was 120/76 and the pulse was 100. The left border of the heart was percussed at the mid-clavicular line. No thrill was noted. There was a low-pitched, systolic murmur of maximum intensity at the apex. A few rales were heard in the right lung base. The electrocardiogram showed changes indicative of an acute anterolateral infarction. The sedimentation rate was moderately elevated. During hospitalization he had occasional bouts of substernal and left chest pain. He died quietly early in the morning of his fifth hospital day.

Autopsy revealed the distended pericardial sac containing a large amount of freshly-clotted blood. It weighed 800 grams. There was a 15 x 5 mm. rupture of the lateral aspect of the left ventricular wall. The surrounding myocardium was necrotic and hemorrhagic. The anterior papillary muscle was torn completely. Its upper portion was 2.5 cm. long and the lower portion 2 cm. The surfaces facing the tear were ragged and hemorrhagic. The tissue of the muscle was soft and yellow-gray to tan. The left circumflex branch showed severe sclerosis with subtotal obliteration of the lumen but without thrombosis. The other branches showed relatively mild changes.

Discussion

Etiology and Pathogenesis: In the great majority of patients, rupture of the papillary muscle is a complication of coronary atherosclerosis and myocardial infarction. It occasionally occurs as a complication of other conditions, such as periarteritis nodosa,[2] syphilis, vegetating valvulitis, and trauma[8] (see Table I).

Infarction in the absence of demonstrable thrombosis is usually explained as resulting from a combination of decreased arterial flow due to arterio-

TABLE I

CAUSES OF PAPILLARY MUSCLE RUPTURE

	Cases
Myocardial infarction with coronary occlusion	42
Myocardial infarction without coronary occlusion	5
Myocardial infarction with normal appearing coronary arteries	1
Periarteritis nodosa	1
Syphilis	1
Probably syphilis	1
Vegetating valvulitis	2
Trauma	6
Unknown	2
TOTAL	61

TABLE II
PAPILLARY MUSCLES INVOLVED

	Cases
Left posterior	37
Left anterior	14
Both left anterior and posterior	3
Right ventricular muscle	2
(Not stated)	6
TOTAL	61

sclerosis plus increased oxygen demand by the myocardium, resulting from some factor such as tachycardia; arteriolar and capillary lesions may also be significant (Barboni and Tumiotto).[9]

Infarction and rupture of the posterior muscle is usually associated with posterior myocardial infarction. Since this type of infarction is variously reported as being from one-half to one-fourth as common as anterior infarction, the posterior muscle would appear to be six to 12 times as susceptible to rupture as the anterior one. The tendency of the posterior muscle to rupture seems to be related to its increased susceptibility to ischemia. Necrosis of this muscle has been demonstrated in 20 per cent of all posterior infarcts,[7] and subendocardial lesions seen in coronary insufficiency were found in greater numbers in the same location.[1] The vulnerability of the papillary muscles in general to inadequate blood supply has been known for a long time. The frequency of scarring in the anterior muscle was referred to by Mönckeberg in 1924.[10] One of us has often seen patches of necrosis and fibrosis in the papillary muscles of young epileptics in correlation with functional disturbances of the circulation and insufficient blood supply to these muscles incident to epileptic attacks and, as a rule, unaccompanied by organic lesions in the arterial tree. The papillary muscles also tend to be involved in carbon monoxide poisoning. The increased susceptibility of the posterior papillary muscle to ischemia may perhaps be explained on the basis of its anatomy and physiology. The blood supply to this area is derived from the right coronary artery[11] or from both main arteries.[24, 25] The vessels that actually supply the posterior muscle, however, are relatively smaller and more remote from their main source than the vessels to the anterior muscle. The demands of the greatly burdened papillary muscles for steady blood supply are considerable. When there are circulatory disturbances, the predominance of necrosis and rupture in the posterior muscle may be explained on the basis of its greater distance from its blood source.

Clinical Picture: The clinical picture of a patient who has just ruptured a papillary muscle is often quite dramatic. A few days or weeks following myocardial infarction, there is a sudden turn for the worse. Breathing becomes labored, the lungs rapidly are filled with moist rales and rhonchi,

and death frequently follows within a few hours to days or even within a few minutes. Associated with this sudden change in the clinical picture is the appearance of a loud apical systolic murmur which was not present before. The murmur is often of a rough or vibratory nature and is usually heard over the entire precordium, but is loudest at the apex and is transmitted toward the axilla. Murmurs were described in only 62 per cent of the reported cases. Their absence in many instances may be attributed to the suddenness of death or to the presence of loud wheezes and rales which obscure heart sounds. However, Askey[1] has cited patients who were closely examined shortly before death and in whom heart sounds were present but no murmur was heard.

Diastolic murmurs have been observed in a few instances. A "friction rub" has been described in five cases. These, however, have not met all of the criteria of a true pericardial friction rub and autopsies have not disclosed evidence of pericarditis. A thrill associated with the murmur has been reported in only one instance and this was a case of incomplete papillary muscle rupture.[3]

In the presence of the clinical picture described, electrocardiographic evidence of a posterior myocardial infarction furnishes some evidence pointing to a ruptured posterior papillary muscle. Conduction disturbances in the electrocardiogram are rare.

Diagnosis of a rupture of the papillary muscles depends upon three factors: 1. Presence of heart disease, most commonly posterior myocardial infarction; 2. Sudden appearance of either a new murmur at the apex or a considerable intensification of an old apical murmur; and 3. Sudden change in the clinical course with the rapid onset of intractable pulmonary edema. To date, only seven of the 61 reported cases in the literature have been diagnosed antemortem including one case in this paper.

TABLE III
SURVIVAL TIME FOLLOWING PAPILLARY MUSCLE RUPTURE

	Cases
Sudden death, less than one hour	11
Less than twenty-four hours	22
Less than one week	1
Less than two weeks	4
Less than two months	4
Four months	1
Six months	1
Ten months	1
Twenty months	1
(Survival unknown)	5
TOTAL	61

Prognosis: Following the rupture of a papillary muscle the outlook is extremely grave. More than 50 per cent of the patients died within the first 24 hours. One-third of them died almost immediately. Less than 20 per cent survived the second week, and only four lived beyond two months (Table III). The only survival beyond one year is Mérat's patient who died 20 months following rupture. In this patient, however, rupture was not due to myocardial infarction.

The cause of death in the majority of these patients is acute left heart failure with intractable pulmonary edema. This is caused by the additional load of severe mitral insufficiency suddenly superimposed upon an already weakened left ventricle. The regurgitated blood markedly increases the left atrial pressure and the blood backs up into the pulmonary circulation. The result is massive pulmonary edema followed shortly by death.[13] Pulmonary edema was a significant finding in four of our cases. In the fifth, it was difficult to evaluate the amount of edema due to the extensive bronchial pneumonia.

An unusual type of death was presented in our fifth case. While rupture of the heart wall was stated to be the cause of death in 9 per cent of all deaths from acute myocardial infarction,[14] such rupture coincident with rupture of a papillary muscle must be extremely rare. We have not been able to find any mention of this in the literature.

Differential diagnosis: After myocardial infarction, rupture of a papillary muscle is most likely to be confused with acute cardiac dilatation with mitral insufficiency. The pictures are quite similar and the sudden onset of failure is likely to be considered as the result of an extension of the infarction. With failure the increase in heart size is often progressive rather than abrupt and the murmur increases in intensity over a period of a few days. Similarly the onset of symptoms in failure is likely to be more gradual than in the case of rupture of a papillary muscle. If infarction is posterior, one should suspect a ruptured papillary muscle in any case where there is a sudden deterioration in the clinical picture of the patient.

Perforation of interventricular septum may resemble rupture of a papillary muscle in its clinical appearance on occasion. Both of these complications occur in the first week or two following the infarction. The murmur of the perforated septum, however, is best heard along the left sternal border in the fourth or fifth interspace. The murmur of a ruptured papillary muscle is that of mitral insufficiency and is best heard at the apex. It is transmitted toward the axilla. A systolic thrill over the left sternal border is present in more than half of the septal perforations, while a thrill has been reported only once in papillary muscle rupture. Anterior myocardial infarction is found in 75 per cent of the cases of septal perforation, while posterior infarction is just as common among cases of papillary muscle rupture. Conduction defects, particularly right bundle branch block, are seen in over one-third of the septal perforations and are rare with papillary muscle rupture. The course following rupture of a papillary muscle is usually rapid with intractable pulmonary edema and left heart failure.

Septal perforation may follow a similar pattern, but is more likely to be associated with a gradually developing failure.[15]

SUMMARY

1. Five cases of papillary muscle ruptured are presented.

2. Rupture of the posterior papillary muscle of the left ventricle is much more common than rupture of the anterior one. The syndrome of simultaneous infarction of the posterior wall of the left ventricle and the posterior papillary muscle with rupture of the latter is described and discussed.

3. Diagnosis of rupture of the papillary muscle should be considered in the presence of acute myocardial infarction, most commonly posterior, when there suddenly develops a loud apical systolic murmur with sudden onset of dyspnea and pulmonary edema.

4. The prognosis is extremely poor.

5. The coincidental occurrence of rupture of the left ventricular wall and of the anterior papillary muscle is reported.

RESUMEN

1. Se presentan cinco casos de ruptura de los músculos papilares.

2. La ruptura del músculo papilar posterior del ventrículo izquierdo es mucho más común que la ruptura del anterior. El síndrome de infarto simultáneo de la pared posterior del ventrículo izquierdo y del músculo papilar posterior con ruptura de éste se describen y se discuten.

3. El diagnóstico de ruptura del músculo papilar debe plantearse en presencia de infarto agudo del miocardio, más a menudo posterior, cuando se presenta de pronto un murmullo sistólico elevado, apical con repentino principio con disnea y edema pulmonar.

4. El pronóstico es malo en extremo.

5. Se refiere la coincidencia de ruptura de la pared ventricular izquierda y del músculo papilar anterior.

RESUME

1. Les auteurs présentent cinq cas de rupture d'un pilier.

2. La rupture du pilier postérieur du ventricule gauche est plus fréquente que celle du muscle antérieur. Le syndrome d'infarctus simultané de la paroi postérieure du ventricule gauche et du pilier postérieur avec rupture de celui-ci est décrite et discutée.

3. On devrait avoir présent à l'esprit le diagnostic possible de rupture du pilier en présence d'infarctus du myocarde, le plus souvent postérieur, lorsque se développe brusquement un souffle systolique de pointe, avec apparition soudaine de dyspnée et d'oedème pulmonaire.

4. Le pronostic est extrêmement grave.

5. Les auteurs rapportent un cas de rupture de la paroi du ventricule gauche coïncidant avec la rupture du pilier antérieur.

ZUSAMMENFASSUNG

1. Fünf Fälle von Ruptur eines Papillarmuskels werden vorgestellt.

2. Eine Ruptur des hinteren Papillarmuskels des linken Ventrikels kommt viel häufiger vor als die Ruptur des vorderen. Beschreibung und Besprechung des Syndroms von gleichzeitiger Infarktbildung der Hinterwand des linken Ventrikels und des hinteren Papillarmuskels mit Ruptur des letzteren.

3. Die Diagnose der Ruptur des Papillarmuskels muss in Erwägung gezogen werden bei Vorliegen einer akuten, meist posterioren Myocard-Infarzierung, sobald sich hier plötzlich ein lautes apikales systolisches Geräusch entwickelt mit plötzlichem Auftreten von Dyspnoe und Lungenoedem.

4. Die Prognose ist äusserst ungünstig.

5. Bericht über gleichzeitizes Auftreten einer Ruptur der Wand des linken Ventrikels und des vorderen Papillarmuskels.

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Case Report Section

Cylindroma of the Breast With Pulmonary Metastases*

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Cylindroma of the breast occurs rarely. Among 2,623 malignant breast tumors, Geschickter[1] found four such cases. More commonly, this tumor arises in the salivary glands, the oral cavity and the tracheo-bronchial tree.[2, 3, 4, 5]

There has been considerable confusion with regard to pathology and biologic behavior of these tumors. They have been classified variously as adenocarcinoma, mixed tumor, basal cell carcinoma, adenocystic carcinoma, carcinoid and others. This arises largely from the lack of complete agreement with regard to the histogenesis of the tumor.

Almost 100 years ago, Billroth used the term "cylindroma" to describe a tumor of the paranasal sinuses that was formed of cylinders of hyaline connective tissue between which lay a network of tumor cells. Subsequently, the term was employed to identify a form of adenocarcinoma of the salivary glands.[6] Various origins have been ascribed to the cylindroma arising in the trachea and bronchi: fetal bronchial buds, the basal layer of the epithelium, the mucous glands and excretory ducts.[7, 8, 9]

In a study of cylindroma of the palate, Bauer and Fox[3] described two types of cells composing the epithelium of the isthmus and ducts of the mucous glands: cylindric cells and basket (basal) cells. The latter are located between the cylindric cells and the basement membrane as well as between the cylindric cells themselves. The basket cells have also been termed myo-epithelial cells because they are supposed to be capable of contracting and thereby facilitating movement of secretion into the excretory ducts. Bauer and Fox concluded that the basket or myo-epithelial cells formed the bulk of the parenchyma of the cylindroma and suggested the name "adenomyoepithelioma." The fibrous stroma which radiates from the capsule invades the tubular epithelial formation and is converted into a hyaline substance by coming into contact with the secretion.

Myo-epithelial cells are found in albuminous glands, mammary glands, glands of Moll and apocrine sweat glands.[10] In the mammary gland, they appear as elongated, spindle shaped cells which lie between the epithelium of the excretory ducts and basement membrane. It is believed that these cells may proliferate either alone or in conjunction with the usual epithelium especially in breasts showing mastopathia cystica or fibroadenomatosis.[11]

The epithelial element of the cylindroma is composed of small, regular, darkly staining cells which are arranged in either a tubular or acinar pattern. The stroma is formed of varying combinations of myxomatous

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or hyalinized connective tissue. Mitoses are rare and the general picture is one of uniformity.

There has also been considerable diversity of opinion with regard to the biologic behavior of the cylindroma. It has been classified as definitely benign.[12] Others have described it as generally benign but with the potentiality of occasional malignant change.[3, 11, 13] It has been considered locally invasive and frequently associated with distant metastases.[2]

The case to be reported is felt to be of interest not only because of the

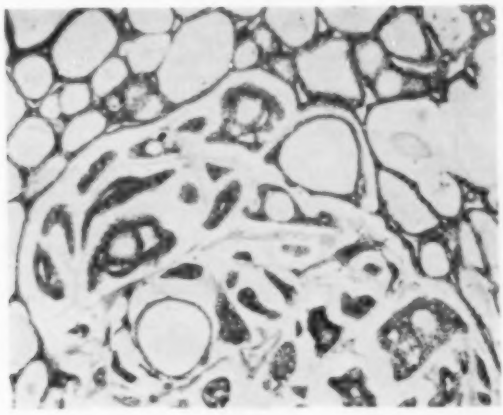

FIGURE 1: Section of cylindroma of breast showing typical arrangement of small, dark staining cells with intervening stroma.

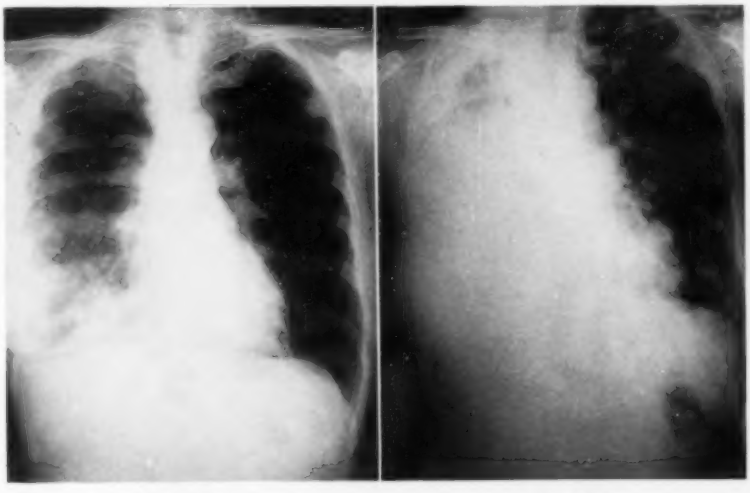

FIGURE 2 FIGURE 3

Figure 2: March 15, 1948. Numerous tumor nodules are present throughout the right lung. The right pleura presents the thickened scalloped appearance associated with tumor invasion. A single nodule is seen in the left upper lung field.—*Figure 3:* Almost complete opacification of the right chest. Numerous nodules are scattered throughout both lungs.

rarity of cylindroma of the breast but also because it illustrates clearly the life history of this tumor.

Case Report: The patient was a single, white, female bookkeeper who first came under my observation in September, 1951. In the Spring of 1939, at the age of 39 years, she had noted a painless lump in the left breast. In March, 1940, she had consulted a physician who confirmed the presence of a mass in the left breast. At that time, she gave a history of recent meno-metrorrhagia. She was immediately hospitalized and a left radical mastectomy was carried out. The pathological diagnosis (Dr. Paul Klemperer) was cylindroma (Figure 1); the lymph nodes were uninvolved. Dr. James Ewing examined the slides and concurred in the diagnosis. Post-operative recovery was satisfactory.

Meno-metrorrhagia persisted and 15 months after mastectomy she was subjected to dilatation and curettage followed by radium insertion. Despite this, irregular bleeding continued for the next three years when menses ceased. In 1943, she complained of vague shoulder and hip discomfort; roentgenograms were negative. In 1945, roentgenograms of the hips were again negative for metastases. Meanwhile, she maintained generally good health and carried on her usual activities.

In March, 1948, moderate dyspnea on exertion was first reported. Chest roentgenogram (Figure 2) disclosed numerous nodules throughout the right lung with some involvement of the left side. Despite this, she maintained her weight and strength and was able to continue working. During the next two years, there was progressive increase in lung findings. In March, 1950, she complained of severe right shoulder pain; roentgenograms were negative. Radiation therapy to the right humerus was administered with little relief.

Testosterone injections (200 to 300 mgm. weekly) were started in March, 1950, and continued until January, 1951. She experienced subjective improvement but there were no objective changes. Voice changes and facial hirsutism developed and estrogen was begun. Increasing weakness, dyspnea and weight loss forced her to take to bed by February, 1951. In April, 1951, right chest tap was attempted at another hospital. The pleura was described as markedly thickened and indurated; no fluid was obtained.

FIGURE 4: Material obtained by aspiration of pleural fluid from left chest: fibrin, red blood cells and cluster of hyperchromatic cells suggestive of a cylindromatous arrangement

When I first examined her in September, 1951, she appeared almost cachectic. Facial hirsutism was present. The entire right chest was flat to percussion with bronchial breath sounds at the base. Scattered crackles were heard on the left. The mastectomy scar was well healed. The remainder of the physical examination showed no abnormality. Chest roentgenogram (Figure 3) revealed extensive changes in both lungs. Estrogen was discontinued in October, 1951.

In February, 1952, she was hospitalized because of increasing dyspnea. Signs of pleural effusion were present on the left side. Chest aspiration yielded 300 cc. of sero-sanguineous fluid; dyspnea remained essentially unchanged. The pleural fluid contained clusters of hyperchromatic cells suggestive of a cylindromatous arrangement (Figure 4).

After she returned home, she was almost completely bed-ridden. For a short period, she received ACTH injections intramuscularly with no apparent effect. On March 20, 1952, 13 years after the breast tumor was first discovered, she died at home. Autopsy was not obtained.

Discussion

This case record illustrates the biologic behavior of which this tumor is capable. Progression was extremely slow. Signs of metastases did not appear until eight years after removal of the primary tumor and the patient survived for four years in the presence of extensive pulmonary involvement. Also of interest is her relative well being for almost three years after the lungs showed widespread metastases. The metastatic deposits were apparently confined to the lungs and pleura although, in the absence of an autopsy, this cannot be stated with certainty. The pulmonary foci were completely unaffected by both male and female sex hormones and adrenocorticotropic hormone.

Although differences from the more common types of malignant tumors exist, nevertheless, it would appear that the cylindroma should be considered always as a basically malignant lesion and should be treated early and radically. While this tumor, in some instances, does not metastasize distantly, it is obviously impossible to predict this in the individual case. In spite of radical mastectomy in our patient, progression to a fatal outcome occurred.

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Primary Pulmonary Leiomyosarcoma

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A review of the literature[1-21] reflects the rarity of primary, smooth-muscle-cell tumors of the lung. Of a total of 24 such tumors reported since the turn of the century, 16 were leiomyosarcomas (Table I) and eight benign leiomyomas (Table II).

Case Report

J. R., a 19-year-old white male farmer, was first seen on June 7, 1954, for complaints including weakness, anorexia, and loss of 35 lbs. weight since March, 1954. Although a recent posterioanterior chest film had been reported as normal, chest x-ray film was repeated, revealing a large round tumor mass with small nodular extensions (Fig. 1), all of which had been previously hidden by the cardiac shadow. A left lateral x-ray film of the chest localized this mass in the left lower lobe behind the heart.

The patient suddenly became dyspneic and developed signs and symptoms of severe internal hemorrhage. X-ray films now showed the left hemithorax to be opaquely blurred with some shift of the mediastinum to the right (Fig. 2). Closed (water-sealed) drainage through catheters introduced intercostally resulted in escape of considerable bloody fluid. X-ray film showed opacity of the lower two-thirds of the left lung field with some improvement in the position of the mediastinum, but dyspnea, requiring the administration of oxygen through an intranasal catheter continued. He was given whole blood transfusions and his blood pressure maintained at 120/80. He was started on penicillin, and his oral temperature of 104° fell over a period of a few days to 101°. His pulse rate fell from 150 to 120 per minute. He was unable to void voluntarily (necessitating an indwelling Foley catheter), sweated profusely and complained of dyspnea, weakness and chest and back pain. Bronchoscopy and studies of the bronchial secretions for malignancy were negative.

On June 29, 1954, operation was performed through a standard left thoracotomy incision. The pleural space was filled with an extensive blood clot and some free bloody fluid. Almost as soon as removal of this blood clot was undertaken, the anesthetist reported that free bloody fluid was filling and escaping out of the endotracheal tube. The operator (A.M.T.) introduced his hand blindly through the extensive blood clot to the upper hilar region and compressed the left main stem bronchus there, later applying a Satinsky clamp to this region. The anesthetist was then able to clear the tracheobronchial tree and maintain a satisfactory anesthetic for the remainder of the operation.

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The large, round, nodular tumor mass occupying the lower posterior and medial portion of the left lower lobe was removed *in toto* by left lower lobectomy. An enlarged hilar lymph node was also removed. Frozen section reports indicated that the lymph node showed no evidence of malignancy, but it appeared that the tumor mass itself was probably malignant, although the exact type of malignancy could not be definitely determined at the time. In view of this report, the remainder of the lung was removed. Several small areas of the pericardium, diaphragmatic surface and parietal pleura were selected for biopsy.

The 300 gm. tumor in the left lower lobe measured 11 cms. in its maxi-

TABLE I

MALIGNANT PRIMARY SMOOTH-MUSCLE-CELL PULMONARY TUMORS

Author	Year Reported	Remarks
Neumann[1]	1938	Two cases pulmonary leiomyosarcomas, females, aged 63 and 83. (Autopsies)
Brunn et al[2]	1940	Leiomyosarcoma, left lower-lobe bronchus, 55 year old male. (Patient refused operation; died of the disease)
Randall et al[3]	1946	Leiomyosarcoma, right lung, 34 year old Negro. (Died during operation for removal of tumor)
Holinger et al[4]	1950	Myosarcoma, anterior wall of trachea, five year old white female. (Successfully removed)
		Myosarcoma, right main bronchus, six-year-old white female (Died after roentgen-ray therapy)
Mishkin[5]	1951	Myosarcoma, left lung, 64 year old white female. (Patient refused operation; died of the disease)
Johnson et al[6]	1952	Leiomyosarcoma, right upper lobe, 52 year old white male. (Successfully treated by pneumonectomy)
Killingsworth et al[7]	1953	Leiomyosarcoma, left lower lobe, seven year old white female. (Successfully treated by pneumonectomy with partial excision of left atrium)
Watson et al[8]	1954	Six cases, pulmonary leiomyosarcomas. (3 successfully treated by surgical excision)
Rosenberg et al[9]	1955	Concurrent leiomyosarcoma and carcinoma, right bronchus, 62 year old white male. (Treated by pneumonectomy)

mum diameter (Fig. 3). It was non-encapsulated but separated easily from the surrounding lung leaving a shallow ragged depression. The cut surface of the tumor was homogenous and of mottled yellow-brown color.

Spindle cells predominated an interlacing pattern, with variations in-

FIGURE 1

FIGURE 2

Figure 1: Posterior-anterior roentgenogram of chest showing large round tumor mass with small nodular attachments extending beyond left cardiac border.—*Figure 2:* Posterior-anterior roentgenogram of chest showing opacity of entire left hemithorax with shift of mediastinum to the right.

FIGURE 3

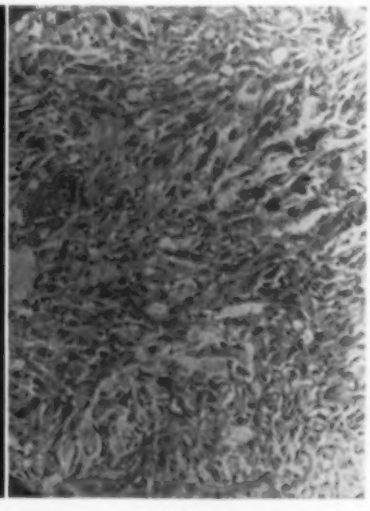

FIGURE 4

Figure 3: Tumor mass in left lower lobe.—*Figure 4:* Photomicrograph of operative specimen (Figure 3) showing interlacing pattern of predominantly spindle cells.

cluding ovoid, ribbon and tumor giant cells (Fig. 4). With von Gieson's stain the tumor cells took a yellow color. When stained with phosphotungstic acid hematoxylin, some of the elongated cells exhibited blue myoglial fibrils.

The remaining lung tissue showed hyperemia. The bronchi showed no significant pathologic change. The additional specimens (hilar lymph nodes, a segment of pericardium, pleura and the remainder of the left lung) showed no involvement by the tumor.

Discussion

Opinion among the pathologists varied as to the malignant potential of this type of tumor. It was pointed out that some of the more benign types of uterine myomata have been proved to metastasize while the more pleomorphic varieties apparently can remain localized for long periods. Expert opinion on this tumor's microscopic picture favored the probability that this was a benign tumor.[22]

TABLE II

BENIGN PRIMARY SMOOTH-MUSCLE-CELL PULMONARY TUMORS

Authors	Year Reported	Remarks
Forkel[10]	1910	Leiomyoma, left upper lobe, 63 year old female. (Autopsy)
Deussing[11]	1912	Multiple primary pulmonary myomas, 57 year old female. (Autopsy)
Franco[12]	1929	Voluminous leiomyoma, right upper lobe, male. (Autopsy)
Brahdy[13]	1941	Fibroleiomyoma, 22 year old female, right lower lobe. (Successfully treated by resection of lower two-thirds right lower lobe)
Williams et al[14]	1950	Leiomyoma, left lower lobe, eight year old female. Youngest patient in series of benign tumors. (Successfully treated by pneumonectomy)
Turkington et al[15]	1950	Leiomyoma, left lower lobe, 57 year old female. Only case diagnosed preoperatively by bronchoscopic biopsy. (Successfully treated by pneumonectomy)
Freireich et al[16]	1951	Leiomyoma, right upper lobe, 61 year old male. (Successfully treated by pneumonectomy)
Pierce et al[17]	1954	Leiomyoma, 24 year old white male, right middle lobe. (Successfully treated by lobectomy)

The immediate and early post-operative course was uneventful and the patient was discharged from the hospital on the 12th post-operative day. He appeared to be in excellent health when, four months after operation, two hard, freely movable, painless subcutaneous nodules approximately 2 cms. in diameter were noted—one in the left anterior abdominal wall and the other on the right thigh. These lesions increased in size, one extending to the skin surface where an ulceration 2 cm. in diameter developed. In December, 1954, this ulcerated lesion was excised, revealing a 3.5 cm. tumor mass, light red and soft to rubbery. Microscopic examination (Fig. 5) showed a pleomorphic tumor, more highly undifferentiated in most areas than the resected pulmonary lesion, composed of solid sheets of fairly large round to ovoid cells, with wide areas of necrosis present throughout the tumor tissue. A few areas showed spindle-shaped cells resembling those seen in the tumor removed from the lung.

Although he continued to feel well for several months, he lost weight and eventually complained of chest pain, weakness and some shortness of breath. On December 6, 1954, a chest x-ray film (Fig. 6) revealed several metastatic nodules in the remaining lung. Early in March, 1955, he was again hospitalized when a large mass was visible and palpable in his right thigh. He died on March 22, 1955.

Autopsy Findings: A soft, white, well-circumscribed, extremely friable tumor extended through the intercostal spaces at the level of the stump

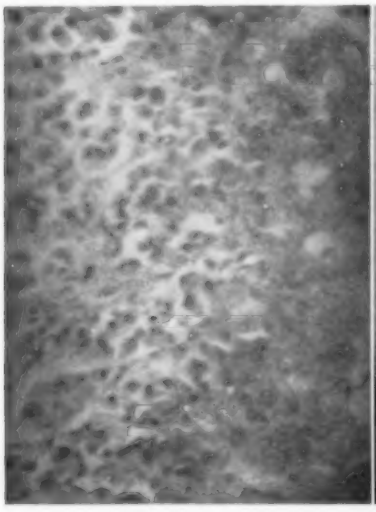

FIGURE 5

FIGURE 6

Figure 5: Photomicrograph of excised subcutaneous nodule showing pleomorphic undifferentiated round to ovoid cells with necrotic areas.—*Figure 6:* Posterior-anterior roentgenogram of chest after left pneumonectomy showing metastatic lesions in right lung.

of the sixth rib (which had been partially removed when the left pneumonectomy was performed). This tumor, palpable externally as a small mass beneath the intact skin, was an extension of similar tumor tissue filling the left pleural space, firmly adherent to the left chest wall, to the diaphragm and to the apex of the chest cavity. Two well circumscribed large nodules, each approximately 8 cm. in diameter and showing areas of necrosis, were present within this intrapleural mass of malignant tissue. Some blood was present in the left pleural space. The fatty tissue surrounding the pericardial sac showed infiltration by the firm pale white tumor tissue, which appeared well-circumscribed. The heart, somewhat dilated and enlarged, with cloudy swelling of the myocardium, was shifted to the left. The enlarged right lung contained two pedunculated tumors on its surface, and five other tumor masses within the lung substance varying from 2 to 8 cms. in size. These soft white well-circumscribed tumors, the larger of which showed central necrosis, could be freely shelled out of the surrounding hemorrhagic lung tissue. The enlarged tracheobronchial lymph nodes on the right side showed evidence of tumor metastases. In the abdomen, the lymph nodes at the head of the pancreas and at the hilus of the liver were enlarged and contained metastatic tumor nodules. The liver weighed 2300 gms., the cut surface showing the mottled red appearance of chronic passive congestion with fatty infiltration. The spleen was also enlarged, the splenic pulp being soft and dark red and the follicles being extremely prominent. The other abdominal organs were essentially normal. Under the fascia of the right thigh was a tumor mass measuring 6 by 9 cms. which could easily be shelled out and appeared to displace rather than infiltrate the muscles.

Discussion

A total of 17 primary pulmonary leiomyosarcomas, including our own, has been reported since the turn of the century,[1-9] nine in females and eight in males, the patients' ages ranging from four to 83 years. The tumors were successfully excised in seven, the surgical procedures varying from local excision of the neoplasm from the trachea[4] or lung,[8] to lobectomies[8] and pneumonectomies.[6, 7, 9] In one, radical pneumonectomy with excision of a portion of the left atrium was necessary to remove the neoplasm.[7] It appears, therefore, that primary leiomyosarcoma of the lung, when localized, may be eradicated surgically. Roentgen ray therapy is also effective as a palliative procedure.

Primary pulmonary leiomyoma has been reported in a total of eight cases,[10-17] five in females and three in males, the ages ranging from eight to 63 years.

The low incidence of benign bronchial tumors in general as compared to malignant tumors can be appreciated by the report by Adams[21] covering a 15 year series totaling 164 cases in which the ratio of malignant tumors was 22 to one. In a review of the literature, Randall and Blades[3] noted the scarcity of reports of mesenchymal tumors of bronchial origin, and particularly of benign tumors arising from smooth muscle.

Acknowledgment: Autopsy was performed on our case and report kindly furnished by Lorin E. Dickelmann, M.D., Pathologist, St. Elizabeth's Mercy and Grace Hospitals, Hutchinson, Kansas.

SUMMARY

A case of a patient with leiomyosarcoma of the lung treated by pneumonectomy is reported. A review of the literature disclosed that 16 such primary pulmonary malignant lesions have been reported, six of which were apparently treated successfully by surgical excision. Leiomyoma, according to the reports in the literature, occurs less frequently, having been reported in only eight cases.

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Hamman-Rich Syndrome
(Diffuse Interstitial Pulmonary Fibrosis)

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In 1935, Hamman and Rich[1] of Johns Hopkins first described a syndrome which they had observed in three patients, characterized by a gradual onset of cough, dyspnea, and cyanosis; and in whose lungs pathologic studies revealed a diffuse interstitial fibrosis, involving the interalveolar septa in particular. In the discussion they emphasized that the causative factors and associated findings commonly seen in the recognized type of pulmonary fibrosis were not found and, indeed, that this was a new entity of unknown etiology.

Since the appearance of their original paper[2-7] and following the appearance of a stimulating editorial in the Journal of the American Medical Association in 1953,[8] approximately 46 additional cases have been reported, of whom 20 have not had all the clinical and pathologic manifestations. An additional case is presented here which conforms to the classical description by Hamman and Rich but in which additional findings of an unusual nature were encountered.

A. L. (USNH OP21609): This 42 year old white woman was admitted to the United States Naval Hospital, Oakland, California, on January 15, 1954, with a history of chronic, productive cough, progressive dyspnea, weight loss, recurrent episodes of spontaneous pneumothorax, and increasing cyanosis of 13 months' duration. She stated she had been in robust health until 18 months prior to admission, at about which time it became evident to her that while she had been athletic in the past, she was experiencing for the first time increasing exertional dyspnea. A pre-employment x-ray film taken one year prior to admission was reported as showing "fibrosis of the lungs" (Figure 1). For the six months prior to admission she became dyspneic even when crossing the kitchen. She recalled that the cough was insidious in onset and was interpreted as "smoker's cough." During this same period she had frequent colds with slight elevations of temperature. Penicillin, streptomycin, terramycin, and combinations of these were used at various times to control a nonproductive cough. The symptoms, however, were not appreciably altered. Careful questioning concerning the inhalation of dusts, etc. in her occupation, environment, and housework failed to elicit any of the agents commonly responsible for pulmonary fibrosis.

Her past and family history were noncontributory.

A bedridden, thin, cyanotic woman, both acutely and chronically ill, weighing 86 pounds, and standing 62 inches. Temperature and pulse were within the limits of normal; respirations, 22 per minute. Blood pressure was 120/80 millimeters of mercury. A few, scattered, fine, moist rales were heard in the lung bases. The vital capacity was 0.7 liters. There was no evidence of clubbing or skin manifestations. The remainder of the physical examination was within normal limits.

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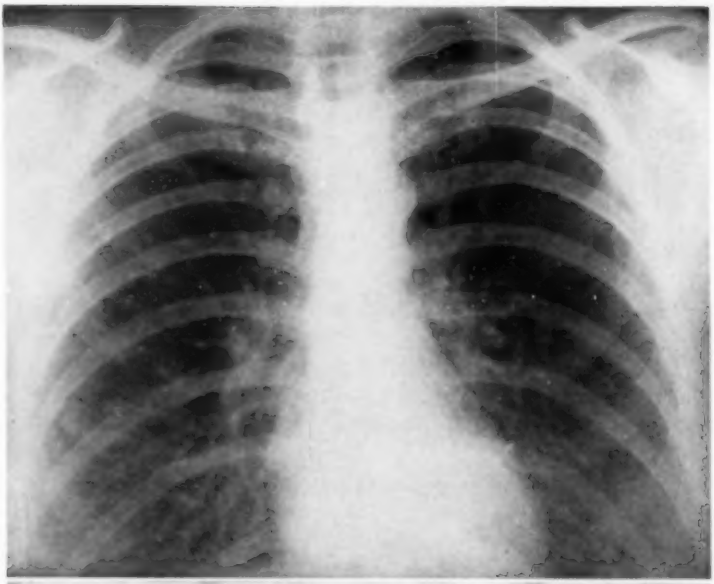

FIG. 1

FIG. 2

Figure 1: A routine pre-employment roentgenogram taken one year prior to hospitalization showing a diffuse, reticular pattern throughout both lung fields. *Impression:* Chronic interstitial fibrosis.—*Figure 2:* Roentgenogram, taken at the time of admission to the U. S. Naval Hospital, Oakland (one year after Figure 1), reveals left pneumothorax and pleural effusion but little significant change in the degree of interstitial fibrosis.

The x-ray films of her chest revealed a diffuse, reticular pattern throughout both lung fields which was interpreted as representing "chronic interstitial fibrosis of unknown etiology." The admission film showed evidence of pneumothorax and minimal pleural effusion of the left side. Comparison with earlier films showed little change. The heart size and configuration were unchanged and within normal limits (Figure 2) X-ray films of the hands were also normal.

Purified protein-derivative tuberculin skin tests both in the first and second strengths (on three occasions) were negative; coccidioidin and histoplasmin skin tests were also repeatedly negative; sputum smears and culture (10 specimens) for acid-fast bacilli and fungi were negative. One routine bacterial smear was found to contain nonhemolytic staphylococcal organisms on culture; however, repeat cultures were negative for predominant bacteria. Repeat Papanicolaou smears for malignant cells in the sputum were negative. Urinalysis and blood Kahn were negative. The white blood cell count was 8,600 with normal differential; hemoglobin, 12 grams; hematocrit, 42 volumes per cent; red blood cells, 4.1 million. The sedimentation rate ranged between 4 and 32 millimeters per hour during the period of hospitalization. The total protein, and albumin/globulin ratio, the blood CO_2 and other electrolytes and two electrocardiograms were within normal limits.

A biopsy of the right paratracheal lymph node was negative. A lung biopsy studied by direct smear and culture for *Coccidioides*, *Histoplasma*, tubercle bacillus, fungi, and inclusion bodies was negative.

She remained confined to her bed throughout most of the hospital stay because of marked exertional dyspnea and, in spite of inactivity and bed rest, she experienced four additional episodes of spontaneous pneumothorax. These crises of pulmonary insufficiency necessitated emergency treatment with needle aspiration, oxygen, intercostal tube, and water-seal bottle. On February 10, 1954 left thoracotomy for parietal pleurectomy (to prevent recurrent collapse) was done. At operation a lung biopsy was obtained, and on the basis of the microscopic findings a diagnosis of Hamman-Rich syndrome was established (Figure 3). The postoperative course was not complicated. On February 23, 1954 she was started on cortisone, 100 milligrams four times daily. This dosage schedule was subsequently reduced to 37.5 milligrams per day.

The clinical course was complicated subsequently by spontaneous pneumothorax on the right and this recurred while a catheter was in the chest. On April 21, 1954 right pleurectomy was performed. Again the postoperative course was not remarkable. However, two weeks following cessation of cortisone therapy she became morose, apprehensive, and cyanotic despite prolonged use of oxygen by tent. Cortisone in the dosage of 37.5 milligrams per day was again started, the need for oxygen was gradually reduced, and she rapidly improved mentally. By July 10, 1954, however, there was evidence of progressive, generalized, peripheral edema which did not respond to vigorous therapy and she expired in pulmonary insufficiency on July 15, 1954.

Autopsy observations will be limited to the heart and lungs since the remainder of the examination was not unusual. The lungs were cyanotic as was the entire body. Shaggy adhesions were observed between the lungs and chest wall except for a small apical and basal pneumothorax on the right. The lungs were of equal weight, totaling 1200 grams. On cut section they had a honeycombed appearance as the result of the many emphysematous blebs (Figure 4). Blood vessels stood out with a somewhat everting, erectile appearance in some focal areas. The bronchi and bronchioles when opened contained a small amount of watery, viscous, reddish fluid. The lymph nodes were not unusual. The heart was of normal size, weight and configuration. The right ventricular wall measured 0.3 to 0.4 centimeters in thickness, while the left ventricle averaged 1.0 centimeters. The valves were normal.

Microscopic sections revealed marked distortion of the pulmonary architecture characterized by thickening of the alveolar walls by fibrosis; numerous scattered areas of dense interstitial fibrosis interspersed by areas of emphysema (Figure 5); and hypertrophy of smooth muscle of the bronchi and periarteriolar areas. The thickening of the alveolar walls in some areas was twice normal, whereas in others the walls were so irregularly thickened and nodular that the lumina of many adjacent alveoli were obliterated. The air sacs whose walls were not greatly involved formed blebs. In general the alveolar spaces were empty. An occasional space was filled with an eosinophilic protein material. Red blood cells were rare as were macrophages. Within and surrounding the interstitial fibrotic areas were numerous, round, inflammatory cells, most marked in the perivascular areas. In small focal areas were neutrophilic, polymorphonuclear leukocytes.

DISCUSSION

This patient was unusual in that she experienced no less than six episodes of spontaneous pneumothorax during her last nine months of illness. These

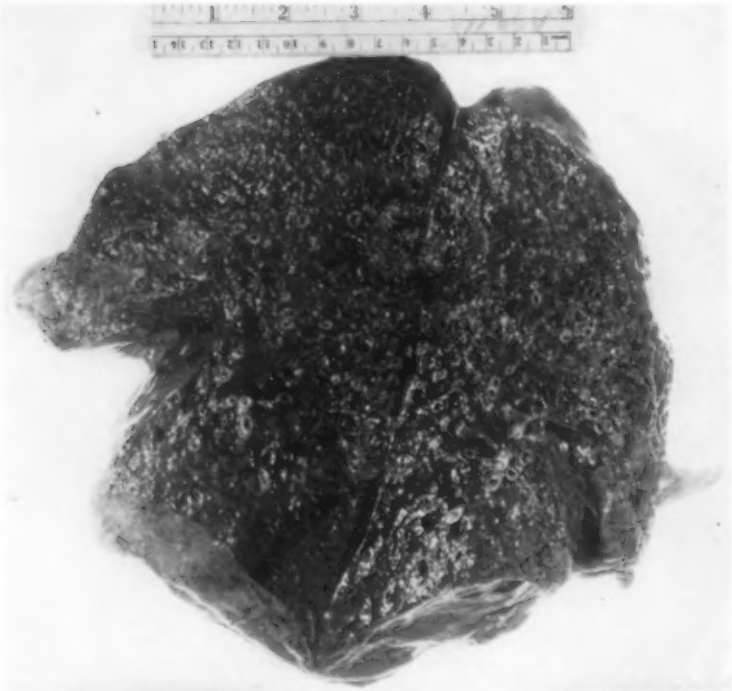

FIG. 3

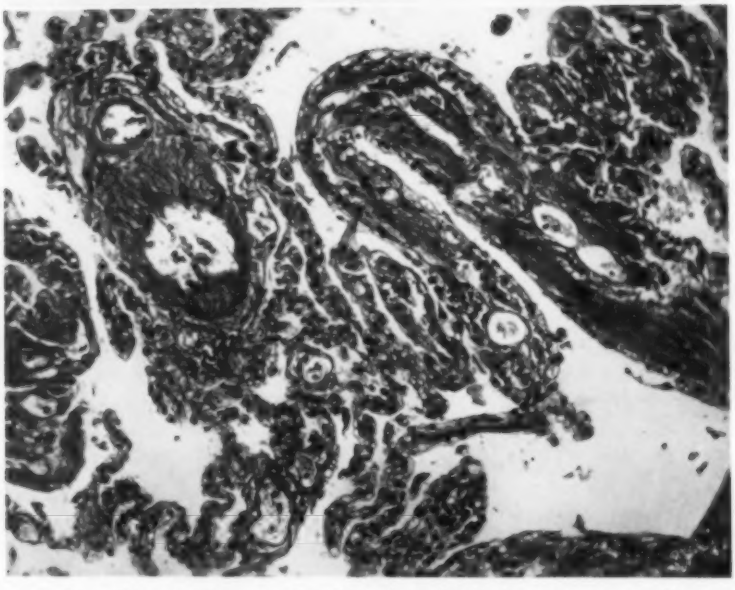

FIG. 4

Figure 3: Lung biopsy taken at the time of parietal pleurectomy revealing marked hypertrophy of the alveolar walls, capillary proliferation, interstitial fibrous reaction, and moderate round-cell infiltration in the interstitial perivascular areas.—*Figure 4:* Cross section of the lung showing a honeycombed appearance as the result of numerous emphysematous blebs.

collapses were subsequently shown to be the result of widespread emphysematous bleb formation. Other observers have described blebs associated with the Hamman-Rich syndrome[5] but without pneumothorax.

Because of recurring bilateral pneumothoraces in a patient already dyspneic, a thoracotomy for parietal pleurectomy and incidental lung biopsy were carried out. At a later date this procedure was repeated on the opposite side. The autopsy demonstrated, as did the clinical course, that the pleurectomy was effective in preventing further episodes of pneumothorax. The small collapses which occurred following operation did so only in the areas where the parietal pleura was left.

At the time of operation it was most interesting to see and palpate the inflated and functioning lung. The surface of the lung was diffusely studded with small blebs, giving a cobblestone appearance. This is well illustrated in Peabody's Case No. 3.[5] The lung was darker than normal, congested, and beefy red. It inflated poorly and deflated slowly. Palpation revealed the increased crepitation of emphysema and the nodular solidarity of bronchopneumonia. Bleeding from the biopsy site was no greater than one sees in the normal individual. The parietal pleura was thickened slightly and was hyperemic.

The use of cortisone was obviously a desperate measure which proved futile; and it seems evident that, as in the cases of Keeton et al.[9] and Peabody et al.,[5] sudden withdrawal of the drug is an extremely hazardous procedure in any patient who has little pulmonary reserve.

Cor pulmonale, as seen in 50 per cent of the previous reports,[5, 10] did

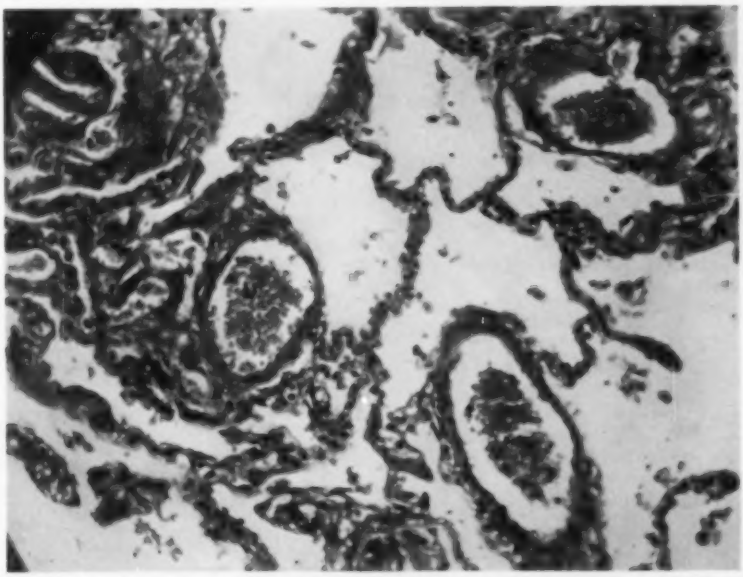

FIGURE 5: Autopsy specimen revealing distortion of alveolar architecture by interstitial fibrosis and rupture of alveolar walls resulting in the pattern of emphysema.

not appear, and the heart size and ventricular walls were normal. There was no evidence of polycythemia reported in many of the previous cases. Thorough questioning regarding the patient's past history, as well as exhaustive laboratory and clinical study, failed to give evidence of known etiologic agents.

Last, the illness of our patient extended over a period of more than 18 months and therefore could not be classed as an acute or fulminating type of disease. Indeed, it would best be placed in the category described by Callahan et al.[6] as chronic interstitial pulmonary fibrosis.

Acknowledgments: The authors wish to express their appreciation for the encouragement and assistance given by Captain Christopher C. Shaw, MC, USN (then Chief of the Medical Service); Doctor Gerald L. Crenshaw, Consultant in Chest Diseases at the U. S. Naval Hospital, Oakland, who was most helpful in the management of this case; and Lieutenant Commander Leonard J. Kreissl, Jr., MC, USNR, who provided the gross and microscopic diagnoses.

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Alveolar Cell Carcinoma of Lung: Report of a Case with Pulmonary Hemorrhage

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Patients with alveolar cell carcinoma of the lung usually expectorate a large amount of white, frothy sputum. This case, characterized as it was by massive pulmonary hemorrhage, therefore is reported as an unusual example of a relatively rare condition.

O. W., a 67 year old Negro farmer, was admitted to the University Hospital December 19, 1955, complaining of coughing up blood. His illness began insidiously two months before with a cough and slight shortness of breath. The cough soon become productive of copious amounts of sputum which was almost pure blood. He estimated that he coughed up as much as eight ounces in one night. Dyspnea became progressively worse and marked weakness was noted.

Bronchoscopy was done at the Mississippi State Sanatorium on December 7, 1955. There was no evidence of endobronchial disease, and the bronchial washings contained many small clusters of cells which were reported as "suspicious of malignant cells."

He had smoked for 50 years but had quit one month before admission. His weight had decreased three pounds in two months. Chills, fever, night sweats, and chest pain had not occurred.

He was a well-developed, well-nourished man who appeared to be chronically ill and who frequently coughed up large amounts of bloody sputum. The vital signs were: temperature 100.2° F.; pulse 86 per minute; respiratory rate 20 per minute; and blood pressure 115/60 mm. Hg. His mucous membranes were pale. A few rhonchi could be heard over the right hilar area but this cleared after coughing. The remainder of the examination revealed normal findings.

The urine was normal. The hemoglobin was 6.2 Gm. per 100 ml. of blood (39.2 per cent) and the white blood cells were 9,500 per cu. mm. with a normal differential count. Total proteins were 5.1 Gm. per 100 ml. of serum with 3.1 Gm. of albumin and 2.0 Gm. of globulin.

X-ray films of the chest were made by Dr. Robert D. Sloan. Posteroanterior and right lateral views revealed diffuse parenchymal mottling of the right lung field in the posteroanterior projection. The majority of these changes appeared to be located posteriorly in the lower lobe, giving it a peculiar stippled appearance. There was no evidence of pleuritic reaction and the diaphragm and bony thorax were normal. This was thought to represent either one of the more uncommon infections or pulmonary adenomatosis.

After admission to the hospital he coughed up 6 to 8 ounces of bloody sputum during each eight hour period. Cytologic studies were reported as "suspicious for malignant cells but unsatisfactory for adequate evaluation."

He was given multiple transfusions, and right pneumonectomy was done December 22. The surgical specimen (Fig. 1) consisted of a right lung, the pleural surface of which was smooth except for a poorly defined depressed area with thickened pleura about 7 cm. in diameter on the posterior surface of the lower lobe. The lung was large and, with the exception of areas anteriorly in the lower lobe, superiorly in the upper lobe, and over most of the middle lobe, was firm. Cut surfaces of the lung were slightly granular and dark red-brown in the consolidated portions, with the exception of being grey and firmer in an area extending about 4 cm. beneath the pleural thickening described above. In the center of this area the tissue was lighter in color and firm; directly adjacent to the pleural surface there were irregular spaces (not shown in the photograph), the largest being about 1.5 by 1.0 by 0.6 cm. The bronchi were not unusual in gross appearance.

Microscopic examination of tissue from the grey firm mass in the lower lobe revealed tumor cells replacing a large part of the lung parenchyma; in areas well away from the pleura the usual pulmonary architecture was seen except for scattered acini lined by the tumor cells. The neoplastic cells varied in size and shape and for the most part were columnar or cuboidal. Nuclei were irregular in size and shape and

From the Departments of Pathology and Surgery, University of Mississippi Medical Center.

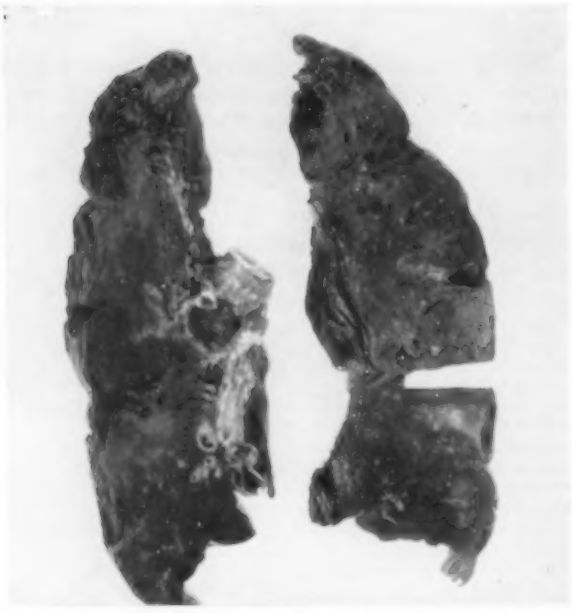
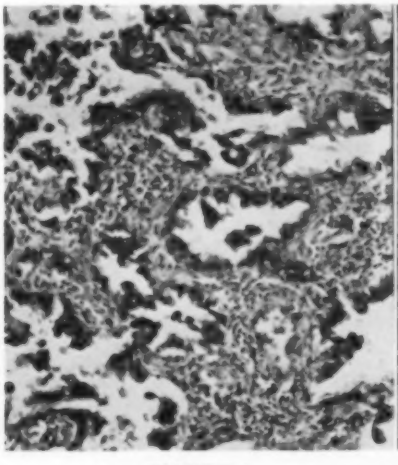


FIGURE 1: (x 2/5) Marked pulmonary hemorrhage is indicated by the very dark areas in each lobe of this fixed specimen, and a part of the tumor can be seen below the missing piece in the lower lobe of the more posterior of the sections.



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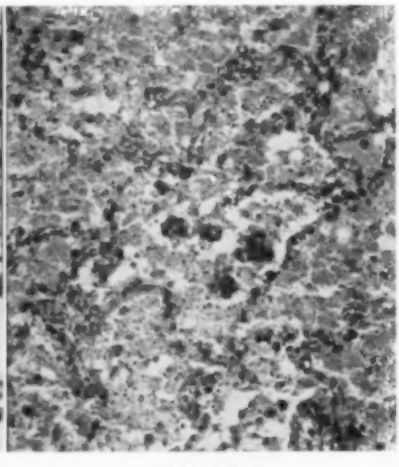

FIGURE 3

Figure 2: (x 140) An alveolar pattern is apparent here in a solid part of the tumor. —*Figure 3:* (x 140) Intra-alveolar hemorrhage is the notable feature in this tissue from the upper lobe, far removed from the primary tumor. The alveolar lining cells are prominent but the very dark irregular material around the septa represents dark brown pigment rather than atypical lining cells. Clumps of cells resembling those of the tumor are present in the air sacs.

varied from vesicular to dark basophilic; scattered mitotic figures were observed. These cells were lining the large spaces noted grossly and in many places were grouped as in Figure 2 to present an irregular alveolar appearance. Many blood vessels contained clumps of tumor cells, and there was an occasional small area of necrosis in other parts of the neoplasm. The stroma in places resembled that of thickened alveolar septa but in other areas was composed of sheets of rather dense fibrous connective tissue containing scattered tumor cells. A few acute and chronic inflammatory cells as well as many red blood cells were seen in the tumor.

Numerous sections taken from other consolidated parts of the lower lobe as well as those taken from similar areas of the other lobes showed red blood cells in many of the alveoli (Fig. 3). Scattered intra-alveolar macrophages containing brown pigment were present. Throughout these areas of pulmonary hemorrhage the alveolar lining cells were swollen, and scattered clumps of cells resembling those of the tumor were lying free in alveoli as in Figure 3. There was no other indication of the presence of neoplasm in these sections.

The bronchi were of normal appearance, and sections of the well aerated portions of lung were characterized by the presence of a few pigment-containing macrophages and scattered red blood cells.

One broncho-pulmonary lymph node contained tumor which resembled that seen in the lung except for a less striking alveolar pattern.

Cultures of the lung were negative for *Mycobacterium tuberculosis* and fungi.

DISCUSSION

The extensive literature on alveolar cell carcinoma was reviewed in 1949 by Swan,[1] in 1952 by Hutchison,[2] in 1953 by Storey, Knudtson, and Lawrence,[3] and recently by Decker.[4]

Our investigation of previous reports on this subject has disclosed none of severe pulmonary hemorrhage. Decker[4] noted that hemoptysis was reported in 13 of 155 cases. Storey, Knudtson, and Lawrence[3] indicated that in 35 of 205 cases included in their statistical analyses hemoptysis was described; however, in only 100 of the cases analyzed was the sputum described by the original contributor. Since a large number of reported cases did not include adequate descriptions of sputum, their belief was that the presence of a small amount of blood in the sputum was more common than their data indicated. To the 35 cases of hemoptysis reported by them the following should be added: six cases described in their summary but for various reasons not included in their statistical analyses; two cases[6, 7] noted by us as having bloody sputum, but not described as such in their summary of cases and therefore apparently not included with the 35 cases of hemoptysis; nine cases mentioned by Watson and Smith[5] without a detailed description of the sputum in each instance; two cases by Farber, Wood and Sangalli[8] and three cases by Decker[4] which have been described since the review in 1953. The above indicates that bloody sputum in this condition is more common than previously thought. However, in most of the reports cited, the sputum was described as "streaked with blood" or characterized by "slight hemoptysis."

The pulmonary hemorrhage in our case may be best explained by the vascular invasion of the tumor at some points and by the focal necrosis in other areas of the tumor. However, the prominent spaces formed within the tumor as previously described could have been responsible for the bleeding. These structures did not appear to be of emphysematous origin but were characterized by an irregular lining of neoplastic cells. Fragile papillary processes protruded into some of the spaces while the central portions of the spaces contained clotted blood.

We prefer the term alveolar cell carcinoma for this tumor, believing that it is of alveolar cell origin without committing us to the exact histogenesis of that cell.

An additional observation of importance in this case was that of clumps of cells similar to those seen in the tumor within alveoli far removed from the nodular mass of the primary neoplasm. These clumps could not be definitely considered growing tumor cells, and therefore this neoplasm was not classified as an example of the diffuse type tumor. However, these clumps of cells do bring to mind the possibility of air-borne metastases through the bronchi. Although not discussed extensively in the literature this route of metastasis has been considered by some authors[2, 3, 8, 9] a mechanism of tumor spread in alveolar cell carcinomas as well as in other tumors.[10, 11] Evidence for this type of metastasis has been supported by the work of Furth in the mouse.[12]

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Spontaneous Perforation of an Oesophageal Diverticulum

*Report of A Case With Survival**

B. H. WEBSTER, M.D., F.C.C.P.
Nashville, Tennessee

Spontaneous rupture of the oesophagus is a medical emergency the outcome of which is often fatal. Although considered rare, 200 cases were collected from the medical literature by Moynihan in 1952. However, the diagnosis of this condition is frequently overlooked or may be made in terminal states or post-mortem. Early detection with surgical repair may mean the difference between survival or death.

Perforation of an oesophageal diverticulum presents the same type of emergency. The present case of a perforation of an oesophageal diverticulum with subsequent development of an acute mediastinitis, a sinus tract leading to the left pleural cavity, and empyema presents several interesting points in differential diagnosis.

Case Report

E. A., a 43 year old white married executive, was well until 30 minutes before admission to the hospital December 3, 1954, following ingestion of a large dinner. Suddenly, he experienced an unbearable crushing substernal pain accompanied by nausea, vomiting, profuse perspiration, faintness, and marked shortness of breath. Examination at the emergency room revealed a well-developed and well-nourished man in shock, cold, clammy, temperature 96.8° F., weak pulse of 128 and blood pressure 84/60. Heart sounds were regular, but distant. Lung fields were clear to auscultation and percussion. The upper abdomen was semi-rigid and somewhat tender. Levuphed and nasal oxygen were administered and the condition improved. The pain persisted and was relieved by opiates.

Past history was non-revealing except for a four months' history of epigastric distress relieved by antacids. There had been no tarry stools.

Upon admission, ruptured peptic ulcer, acute myocardial infarction, acute pancreatitis or ruptured oesophagus were suspected. An upright flat film of the abdomen revealed no free-air beneath the diaphragm. An x-ray film of the chest was normal. An electrocardiogram revealed an occasional auricular premature systole but was otherwise within normal limits. Initial blood studies revealed hemoglobin of 14.0 grams, packed cell volume 42 per cent, leukocyte count 15,100 with 94 per cent polymorphonuclear cells, and sedimentation rate 16 mm. On the following day, fasting blood sugar was 98 mgms. per cent, non-protein nitrogen 30 mgms. per cent, serum amylase 82 mgms. per cent, and serum bilirubin 0.2 mgms. per cent. Serology was negative.

He was dyspneic, experienced considerable tachycardia during the early days of his admission and was critically ill. Temperature was a septic type ranging from 100 to 105° F. daily with frequent chills. Repetition of the flat film of the abdomen was negative on the third day as was also a film of the chest. Lipiodol swallow was non-revealing. Serial electrocardiograms during a period of 30 days were normal. The leukocyte count ranged from 15,000 to 26,500 with a high polymorphonuclear leukocyte count. The sedimentation rate rose to 38 mm., serum amylase ranged 50 to 88 mgms. per cent, urinalysis was negative. Stools were negative for occult blood. A tuberculin test 1.1000 was negative.

On the seventh hospital day (December 8, 1954), he was found to have flatness to percussion over the lower left lung field and absent breath sounds (Figure 1). An x-ray film of the chest for the first time revealed a small left pleural effusion. Thoracentesis yielded 30 cc. of a thin, yellow purulent fluid which upon culture revealed

*From the Department of Internal Medicine, Mid-State Baptist Hospital, Nashville, Tennessee.

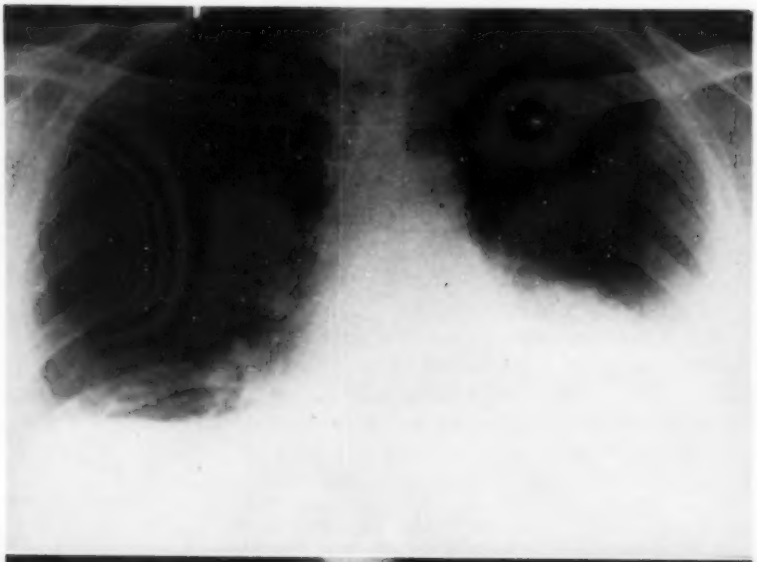

FIG. 1

FIG. 2

Figure 1: December 8, 1954, x-ray film of chest, revealing a small left pleural effusion.—*Figure 2:* January 3, 1955. gastro-intestinal series, showing a diverticulum of the distal end of the oesophagus and oesophageal hiatal hernia.

Hemolytic Staphylococcus albus. Sensitivity tests were positive for erythromycin. Culture of the fluid was negative for *M. tuberculosis* and guinea pig inoculation was negative at the end of six weeks. Sputum examination was negative for *M. tuberculosis* by Ziehl-Neelsen stain and culture. Blood cultures were negative.

The fluid in the left pleural cavity increased, but was gradually relieved by repeated small thoracenteses, but the fluid became so thick that this was no longer possible.

On December 15, 1954, thoracotomy was performed and a drainage tube inserted. There was slight evidence of a widening of the mediastinum on chest x-ray films at this time suggesting mediastinitis. During hospitalization, he received parenteral fluids, transfusions, penicillin, streptomycin, erythromycin, and streptokinase and streptodornase.

Improvement was progressive following thoracotomy and by January 3, 1955, it was thought safe to investigate roentgenologically the gall bladder and upper gastro-intestinal tract. X-ray inspection of the gall bladder revealed normal function without stones. The upper gastro-intestinal series revealed a constriction and a diverticulum of the lower end of the oesophagus, and a small oesophageal hiatal hernia. There was a collection of barium in a cavity adjacent to the lower end of the oesophagus just above the cardiac end of the stomach. At one time during the fluoroscopic examination a small trickle of barium seemed to extend into the apparent diverticulum, denoting a sinus tract just beneath the diaphragm and extending above the diaphragm into the left pleural cavity (Figures 2 and 3). No sign of gastric or duodenal ulcer was present.

On January 5, 1955, the packed cell volume was 44 per cent, leukocyte count 9400, serum amylase 84 mgms. per cent. Stool examination was negative for occult blood. Urinalysis was negative. X-ray film of the chest revealed thickened pleura in the left lower chest area, otherwise normal. Temperature was 98.4° F., pulse 80.

On February 5, 1956, roentgenologic examination of the chest and upper gastro-

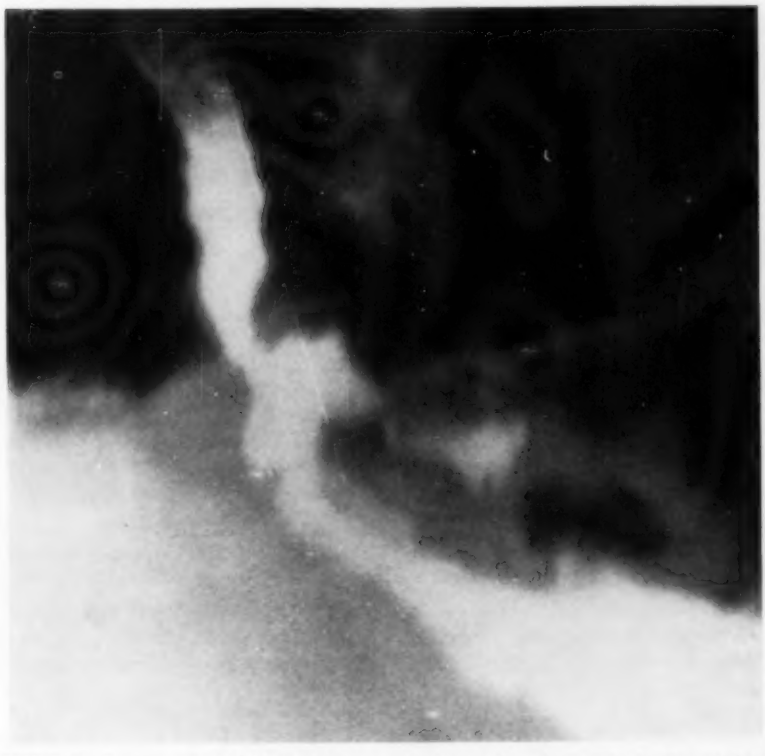

FIGURE 3: January 3, 1955, denoting a collection of barium outside the perforated oesophageal diverticulum and extending to the left pleural cavity.

intestinal series were normal except for demonstration of a small oesophageal hiatal hernia and a small diverticulum of the lower end of the oesophagus.

The final diagnosis was: (1) Ruptured oesophageal diverticulum. (2) Empyema. (3) Acute mediastinitis.

DISCUSSION

This case typifies the sudden onset of spontaneous perforation of the oesophagus with substernal pain, nausea, vomiting, dyspnea, and shock. This was followed by reflex tenderness and distention of the upper abdomen. Only after five days were diagnostic confirmatory signs found.

The conditions most commonly considered in the differential diagnosis are spontaneous pneumothorax, perforated peptic ulcer, myocardial infarction, dissecting aortic aneurysm, acute pancreatitis, and acute oesophagitis. A swallow of 10-20 cc. of lipiodol may frequently reveal a rent in the oesophagus. The typical history such as in this case accompanied by mediastinal emphysema, or fluid in the left pleural cavity may be diagnostic. Recognition in a typical case is easy if the diagnosis is suspected.

Excessive vomiting or severe sneezing may precipitate the condition. Sudden increase in intra-abdominal or gastric pressure by ingestion of a large meal as in this case, excessive drinking or straining at defecation may be the etiology. Case reports have indicated that perforation may follow an epileptic fit, lifting a heavy weight, or direct blows to the abdomen. Rarely, the presence of peptic oesophagitis may lead to necrosis and leakage from the terminal oesophagus. This was experimentally demonstrated by Brackney and his coworkers.

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The President's Page

To the Members of the American College of Chest Physicians:

An outline of the scientific program to be presented at the annual meeting of the College in New York City from May 29 to June 2, 1957, is included in this issue of the journal. It should prove of great interest to all our members, and this is a meeting that no member can well afford to miss. The Committee on Scientific Program, under the chairmanship of Dr. Karl Pfuetze, has devoted much time, thought and energy to assembling a most interesting and instructive program. From the opening session, at which we will have the opportunity to hear famous speakers and international authorities in their chosen fields, through the next 3 days, the same high standards of presentations will be maintained.

The arrangement of a scientific program is, at best, a most difficult assignment. It becomes increasingly difficult and complex as the interests of the audience become more and more diversified. Cognizance must be given also to the fact that information and knowledge which may seem commonplace to some members may be relatively unknown or new to others, but care must be taken to avoid the so-called pot-boiler. The Committee on Scientific Program has earnestly endeavored to consider all these factors at the same time, with the thought of presenting material in such a manner as to keep our membership informed of the latest and best developments in the field of cardiopulmonary disease.

This year a special session will be devoted to a series of short papers given mostly by young investigators, reporting on new developments in the cardiopulmonary field. Other medical societies that have started similar sessions have found them most successful and instructive, for they afford a rapid and excellent method of keeping abreast of the times. I hope that our society will give this session its support, as that will encourage the young investigator and be indicative of the interest of the College in research.

Splendid luncheon meetings and fireside conferences have been arranged, with distinguished speakers and panelists in charge. These luncheon meetings and conferences provide a chance for give-and-take discussion which no other type of meeting permits. In past years, many members have been disappointed that they were unable to gain admission to some of the luncheon meetings. In order to avoid such disappointment, it is suggested that you send in your reservations for the luncheon sessions of your choice as early as possible.

With such an excellent meeting in prospect, may I urge that you make prompt arrangements to be present and that you make early hotel reservations for the accommodations of your choice.

Our thanks are due to Dr. Pfuetze and his Committee for the tremendous amount of work they have done to make the program a success, and to all the other members who have contributed so generously of their time and ability to arrange for this year's meeting.

A. J. Morrisch

REPORT OF THE COMMITTEE ON COLLEGE BYLAWS

Five amendments will be presented to the membership of the College for approval at the time of the open administrative session to be held in New York City, in connection with the 23rd annual meeting of the College, on Saturday, June 1. The amendments are as follows:

Article III, Membership

Section 1: Members of the College shall be of the following classes: *Masters*, Fellows, Fellows Emeritus, Associate Fellows, Associate Members and Honary Fellows. *Masters* and Fellows shall be entitled to all the privileges of the College including the privilege of voting and holding office. *Masters shall be privileged to use the degree "M.C.C.P." after their names*, and only Fellows, Fellows Emeritus and Honorary Fellows shall be privileged to use the degree "F.C.C.P." after their names. Other members shall be entitled to all the privileges of the College except the privilege of voting and the privilege of holding office.

Recommendation: That the italicized words and phrases be inserted in Sec. 1.

Section 3: (c) Associate membership.

(8) The Board of Regents may grant Associate Membership to other worthy individuals who, in the opinion of the Board, merit such recognition.

Recommendation: That the above paragraph (8) be added to Section 3 (c).

Section 3: (f) Masters. Masters of the American College of Chest Physicians shall be those who have attained the rank of Fellow and who have served as President of the College. Other members holding the rank of Fellow may be elected as Masters upon the recommendation of the Board of Regents of the College.

Recommendation: That the above paragraph (f) be added to Section 3.

Article V, Board of Regents

Section 3: The elected members of the Board shall each serve for a term of three years *and no member may serve more than three consecutive terms*, provided, however, that at the first election of the Board approximately one-third of the elected members shall be elected for a one-year term, approximately one-third for a two-year term, and the remaining one-third for a three-year term. The original division of the members into approximate thirds shall be made by the President of the College.

Recommendation: That the italicized phrase in the above section be removed from the bylaws.

Article X, Councils and Committees

Section 1: All councils and committees of the College shall be appointed by the President, who shall designate a chairman, vice-chairman, and secretary of each council and committee. Members of councils and committees shall be both individually and collectively responsible to the Board of Regents for the conduct of their respective organizations. Reports and other publications of all councils and committees *must be submitted to the Executive Council for study* and shall be approved by the Board of Regents before publication.

Recommendation: That the italicized phrase be inserted in Section 1.

Carl H. Gellenthien, *Chairman*
Robert E. Schwartz
Henry J. Stanford

College Chapter News

MISSOURI CHAPTER

The annual meeting of the Missouri Chapter of the College will be held at the Hotel President, Kansas City, on Sunday, March 31. The following program will be presented:

11:30 a.m. Business meeting

12:00 noon Luncheon

"Mucoid Impact of the Bronchi"
Robert R. Shaw, Dallas, Texas

"Rheumatic Mediastinitis a Factor in Persistent Rheumatic Fever"
Graham Asher, Kansas City, Missouri

"Further Experiences with the Surgery of Histoplasmosis"
John W. Polk, Springfield, Charles A. Brasher, Mount Vernon, and W. W. Buckingham, Kansas City, Missouri

"Clinical-Surgical Pathological Conference"
Henry C. Sweany, Charles A. Brasher, and W. W. Buckingham, Kansas City, Missouri

X-ray Conference

TENNESSEE CHAPTER

The Tennessee Chapter of the College and the Tennessee Thoracic Society will meet jointly at the Noel Hotel, Nashville, April 9. After a luncheon and business meeting commencing at noon, the following scientific program will be presented:

1:15 p.m. "Homograft Replacement of Aortic Arch
James Pate and Felix Hughes, Memphis

"Problem with Lye Burns of the Esophagus"
William K. Rogers, Knoxville

"The Treatment of Tuberculosis in Children"
William G. White, Memphis

"Pulmonary Histoplasmosis with Cavitation"
W. W. Hubbard, Nashville

"Indications and Use of Pre-resection and Post-resection Thoracoplasty in Tuberculosis"
Robert W. Newman, Knoxville

"Experience with the Use of Pyrazinamide for Excisional Therapy in the Poor Risk Tuberculous Patient"
Sam E. Stephenson, Nashville

PANAMA CHAPTER

The Panama Chapter will hold a scientific meeting in Panama City, April 5-6, and officers will be elected for the coming year. The meeting will follow the Second Inter-American Medical Convention to take place in Panama City, April 3-5. Dr. Maximo Carrizo Villarreal is acting Regent of the College for the Republic of Panama, replacing Dr. Amadeo V. Mastellari who served as Regent for a number of years prior to his recent demise. The following scientific program has been arranged by Dr. Rodolfo V. Young of Ancon, acting Governor of the College for Panama:

Friday, April 5

6:00 p.m. Dinner

8:00 p.m. Inauguration address
Rodolfo V. Young, Ancon, Rep. of Panama

8:15 p.m. "Surgery in Diaphragmatic Hernia"
William F. Rienhoff, Jr., Baltimore, Maryland

The scientific session will be followed by a social function, sponsored by the Second Inter-American Medical Convention and the Doctors' Wives Club of the Republic of Panama.

Saturday, April 6

8:00 a.m. "Surgery of Pulmonary Tuberculosis"
Hawley H. Seiler, Tampa, Florida

"The Active Management of Pulmonary Tuberculosis in Pregnancy"
Irving J. Selikoff, New York, New York

12:00 noon Luncheon

ARIZONA CHAPTER

The annual meeting of the Arizona Chapter will be held in Yuma, April 12. Dr. Henry D. Brainerd, San Francisco, California, will address the chapter on "The Diagnosis and Treatment of the Pneumonias."

23rd ANNUAL MEETING
AMERICAN COLLEGE OF CHEST PHYSICIANS
HOTEL COMMODORE, NEW YORK CITY

SEMINARS

Wednesday, May 29

Morning Sessions—9:00 a.m.—12:00 Noon

AM-1 PULMONARY DISEASE (MEDICAL)

Chairmen:

Edgar Mayer, Clinical Professor of Medicine, New York University Post Graduate Medical School, New York City

Coleman B. Rabin, Attending Physician for Chest Diseases, The Mount Sinai Hospital, New York; Assistant Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York City

9:00 A.M.—Pulmonary Pathology as a Determinant in Definitive Treatment of Lung Disease

Oscar Auerbach, Associate Professor of Pathology, New York Medical College; Chief, Laboratory Service, VA Hospital, East Orange, New Jersey

9:45 A.M.—The Medical Management of Bronchopulmonary Infections

Alvan L. Barach, Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York City

10:30 A.M.—The Present Status of Antimicrobic Treatment of Tuberculosis

Irving J. Selikoff, Attending Physician, Sea View Hospital; Associate Physician for Chest Diseases, The Mount Sinai Hospital, New York City

11:15 A.M.—The Diagnostic Problems Presented by Diffuse Pulmonary Lesions

Eli Rubin, Professor of Medicine, Albert Einstein College of Medicine; Attending Physician, Pulmonary Division, Montefiore Hospital, New York City

A Ten-Minute Question and Answer Period Will Follow Each Lecture

AM-2 CARDIOLOGY (SURGICAL)

Chairmen:

Charles K. Friedberg, Cardiologist and Attending Physician for Cardiology, The Mount Sinai Hospital; Associate Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York City

Jere W. Lord, Jr., Professor of Clinical Surgery, New York University Post Graduate Medical School; Visiting Surgeon, Bellevue Hospital, Fourth Division, New York City

9:00 A.M.—The Surgical Approach to Coronary Disease and Myocardial Ischemia

Samuel A. Thompson, Associate Professor of Surgery, New York Medical College, New York City

9:45 A.M.—The Value of Cardiac Catheterization in Surgery of the Heart

Regane Harvey, Associate Professor of Clinical Medicine, College of Physicians and Surgeons, Columbia University; Associate Visiting Physician, Bellevue Hospital, New York City

10:30 A.M.—Intracardiac Surgery Through the Open Heart; Hypothermia and Extra-Corporeal Shunt

Ivan Baronofsky, Director of Surgery, The Mount Sinai Hospital; Clinical Professor of Surgery, College of Physicians and Surgeons, New York City

11:15 A.M.—Surgery of Mitral Valvular Disease

Charles P. Bailey, Professor and Head of Department of Thoracic Surgery, Hahnemann Medical College and Hospital; Head of Department of Cardiovascular Surgery, Albert Einstein Medical Center, Philadelphia, Penna.

A Ten-Minute Question and Answer Period Will Follow Each Lecture

Seminars (continued)

Afternoon Sessions—2:00 p.m.—5:00 p.m.

PM-1 PULMONARY DISEASE (SURGICAL)

Chairmen:

Daniel A. Mulvihill, Chief of Thoracic Surgery, Saint Vincent's Hospital, New York City

William Watson, Attending Surgeon, Thoracic Service, Memorial Center; Associate Professor of Surgery, New York University, New York City

2:00 *P.M.—Effect of Lung Function on Morbidity and Mortality of Pulmonary Resection*

Herbert C. Maier, Director of Surgery, Lenox Hill Hospital; Associate Clinical Professor of Surgery, College of Physicians and Surgeons; Columbia University, New York City

2:45 *P.M.—The Radical Operation for Primary Bronchiogenic Carcinoma*

John L. Pool, Associate Attending Surgeon, Thoracic Service, Memorial Center, New York City

3:30 *P.M.—Bronchoscopy in Relation to Medical and Surgical Management of Thoracic Disease*

Chevalier L. Jackson, Professor of Laryngology and Bronchoesophagology, Temple University Medical Center, Philadelphia, Pennsylvania

4:15 *P.M.—Indications and the Late Results of Segmental Resection in Tuberculosis*

J. Maxwell Chamberlain, Assistant Clinical Professor of Surgery, College of Physicians and Surgeons, Columbia University; Attending in Charge of Thoracic Surgery, Roosevelt Hospital, New York City

A Ten-Minute Question and Answer Period Will Follow Each Lecture

PM-2 CARDIOLOGY (MEDICAL)

Chairmen:

Arthur M. Master, Associate Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University; Consultant Cardiologist, The Mount Sinai Hospital, New York City

Irving S. Wright, Professor of Clinical Medicine, Cornell University Medical College; Attending Physician, New York Hospital, New York City

2:00 *P.M.—The Indications and Practical Value of Angiocardiography*

Israel Steinberg, Associate Professor of Clinical Radiology and Assistant Professor of Clinical Medicine, Cornell University Medical College, New York City

2:45 *P.M.—Clinical and Experimental Application of Serum Enzyme Determinations in Heart Disease*

John S. La Due, Associate Attending Physician, Memorial Medical Center; Assistant Clinical Professor of Medicine, Cornell University Medical College, New York City

3:30 *P.M.—The Treatment of Intractable Heart Failure*

Hugh Luckey, Dean, Cornell University Medical College, New York City

4:15 *P.M.—Management of the Heart Patient During Pregnancy*

Simon Dack, Assistant Clinical Professor of Medicine, New York Medical College; Chief, Pre-natal Cardiac Clinic, The Mount Sinai Hospital, New York City

A Ten-Minute Question and Answer Period Will Follow Each Lecture

NOTE: These seminars on diseases of the chest will be presented at the Hotel Commodore on Wednesday, May 29, and are open to all physicians. The seminars have been accredited by the Board of Examiners for candidates for Fellowship in the College. The registration fee for each seminar, which consists of a series of four lectures, is $7.50.

Registration for the seminars must be made in advance and accompanied by the tuition fee; seating capacity is limited and reservations will be accepted in the order received. A coupon for this purpose will be found on page 372. Please indicate your preference by number.

SCIENTIFIC PROGRAM

Thursday, May 30

8:00 p.m.—Scientific Session

SECOND LOUIS MARK MEMORIAL LECTURE

Precordial Noises Heard at a Distance from the Chest, Series II

William B. Bean, Professor and Head, Department of Internal Medicine, State University of Iowa School of Medicine, Iowa City, Iowa

* * *

The Future of Cardiac Surgery

Edgar W. Davis, Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

The Future of Cancer Research

J. R. Heller, Director, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

Speculations on the Treatment and Control of Tuberculosis

H. Corwin Hinshaw, Clinical Professor of Medicine (Diseases of the Chest), Stanford University School of Medicine, San Francisco, California

Friday, May 31

9:00 a.m.—Scientific Session No. I

Symposium on Clinical Cardiology

Arteriovenous Fistula of the Lung

David P. Boyd, Thoracic Surgeon, Lahey Clinic, New England Baptist and Deaconess Hospitals, Boston, Massachusetts

Coronary Insufficiency in Pulmonary Hypertension

Eliot Corday, Assistant Clinical Professor of Medicine, University of California School of Medicine; Herbert Gold, Clinical Instructor, University of California School of Medicine; and Leo Kaplan, Director of Laboratory, Mt. Sinai Hospital, Los Angeles, California

The Hemodynamic and Clinical Characteristics of Rheumatic Aortic Stenosis

Harry Goldberg, Assistant Professor of Medicine; Clarence Denton, Associate in Medicine, Hahnemann Medical College; Sheldon Bender, Fellow, National Institutes of Health; and Joseph Uricchio, Instructor in Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Studies on the Role of Inspiratory Positive Pressure Oxygen Breathing (IPPB-O_2) in the Treatment of Pulmonary Edema

William F. Miller, Assistant Professor of Medicine; Brian J. Sproule, Research Fellow, Internal Medicine; James P. Lillehei, Instructor, Internal Medicine; Nancy Wu, formerly Instructor, Internal Medicine (now in Department of Anesthesiology, Massachusetts Memorial Hospital, Boston); and Ivan E. Cushing, Research Fellow, Internal Medicine, University of Texas Southwestern Medical School, Dallas, Texas

The Surgical Correction of Aortic Insufficiency

Warren J. Taylor, Associate Surgeon, Malden Hospital; Wendell B. Thrower, Surgical Service, Boston City Hospital; Harrison Black, Instructor in Surgery, and Dwight E. Harken, Associate Clinical Professor of Surgery, Harvard Medical School, Boston, Massachusetts

Friday, May 31 (continued)

EKG Conference

Moderator:

Raymond D. Pruitt, Professor of Medicine, University of Minnesota Medical school, Rochester, Minnesota

Panel:

Joseph M. Barker, Beverly Hills, California

Simon Dack, Assistant Clinical Professor of Medicine, New York Medical College, New York City

Jesse E. Edwards, Professor of Pathology, University of Minnesota Medical school, Rochester, Minnesota

Robert P. Grant, Senior Surgeon, National Institutes of Health, Bethesda, Maryland

Questions and discussion from the floor

9:00 a.m.—Scientific Session No. II

Symposium on Tuberculosis (Medical and Surgical)

The Use and Abuse of Steroids in Tuberculosis

Harry Shubin, Chairman, Department of Diseases of the Chest, Philadelphia General Hospital, Northern Division; Robert Lambert, Medical Director, Rush Hospital; Charles A. Heiken, Chief Visiting Physician; and San Singhaphakdi, Resident, Philadelphia General Hospital, Northern Division, Philadelphia, Pa.

Pyridoxine and Isoniazid Induced Neuropathy

William Mandel, Clinical Instructor, University of California School of Medicine, San Francisco, California

Cycloserine-Isoniazid: Data from VA-Armed Forces Cooperative Study

Patrick B. Storey, Assistant Professor of Medicine, University of Maryland School of Medicine; and Ross L. McLean, Assistant Professor of Medicine, John Hopkins University School of Medicine, Baltimore, Maryland

Early Diagnosis and Treatment of Tuberculosis in Children

Edna M. Jones and W. Leonard Howard, William H. Maybury Sanatorium, Northville, Michigan

Tuberculous Dried Cavities (So-Called "Bullous Cavities in Resected Lungs")

J. A. Vidal, Director, Tuberculosis Commission, Province of Quebec; Roland Guy, Anatomo-Pathologist and Director of Laboratories, Hospital du Sacre-Coeur; and B. Guy Begin, Surgeon, Hospital du Sacre-Coeur, Montreal, Canada

Results of the New York City Ambulatory Treatment Program for Tuberculous Patients

Morton H. Aronsohn, Supervisor of Clinics; Hans Abeles, Assistant Director; Joseph Breuer, Supervisor of Clinics; Aaron D. Chaves, Supervisor of Clinics; and Arthur B. Robins, Supervisor of Clinics, Bureau of Tuberculosis, New York City Department of Health, New York City

Mass Tuberculin Patch Testing of School Children (A Critical Analysis of 125,000 Cases)

Walter C. Gray, St. Joseph's and Missouri Baptist Hospitals, St. Louis, Mo.

General Treatment of Tuberculosis

Panel Discussion

Moderator:

Col. James A. Wier, Chief, Pulmonary Disease Service, Fitzsimons Army Hospital, Denver, Colorado

Panel:

Sumner S. Cohen, Assistant Medical Director, Glen Lake Sanatorium, Oak Terrace, Minnesota

Raymond F. Corpe, Superintendent, Battey State Hospital, Rome, Georgia

Eugene T. McEnery, Clinical Professor of Pediatrics, Stritch School of Medicine, Loyola University, Chicago, Illinois

Henry C. Sweany, Director of Research, Pathology and Allied Sciences, Missouri State Sanatorium, Mount Vernon, Missouri

Questions and discussion from the floor

Friday, May 31 (continued)

12:00 noon—Round Table Luncheon Discussions (see page 364)

2:00 p.m.—Scientific Session No. 1

Forum on Basic Research in Diseases of the Chest: Pulmonary

Steroid Acid Amides of Diamino Diphenyl Sulfone in Tuberculosis

Arpad Berczeller, Director of Bacteriology, Sea View Hospital, Staten Island, New York City

Pulmonary and Circulatory Effects of Acute Pulmonary Vascular Engorgement

Stuart Bondurant, USPHS Post Doctorate Research Fellow; and John B. Hickam, Associate Professor of Medicine, Department of Medicine, Duke University Hospital, Durham, North Carolina

Cardiorespiratory Studies in Hamman-Rich Syndrome

Peter Luchsinger, Instructor in Medicine, Georgetown University School of Medicine; Sol Katz, Adjunct Clinical Professor of Medicine, Georgetown and George Washington Schools of Medicine; Georges McCormick, Associate Professor of Medicine; and Robert Donohoe, Instructor in Medicine, Georgetown University School of Medicine, Washington, D. C.

Electrolyte Abnormalities in Pulmonary Emphysema Before and After the Administration of Diamox

David M. Kydd, Associate Professor of Medicine; and Harold A. Lyons, Associate Professor of Medicine, State University of New York College of Medicine, Brooklyn, New York

Considerations in Humidification by Nebulization

Ivan E. Cushing, Research Fellow, Internal Medicine; and William F. Miller, Assistant Professor of Medicine, University of Texas Southwestern Medical School, Dallas, Texas

Physiological and Pharmacological Factors Influencing Collateral Blood Flow to the Lungs ("Bronchial Flow")

Peter F. Salisbury, Principal Investigator, Institute for Medical Research; Peter Weil, Research Fellow, Department of Surgery; and David State, Director of Surgery, Cedars of Lebanon Hospital, Los Angeles, California

The Topographic Distribution of Mineral Dusts in Some Pneumoconiotic Lungs

Paul Gross, Research Pathologist, Industrial Hygiene Foundation; and Kenneth W. Smith, Medical Director, Johns-Manville Corporation, Pittsburgh, Penna.

Differentiation of the Causes of Pulmonary Hypertension in Mitral Stenosis by Simultaneous Right and Left Heart Catheterization

Philip Samet, Assistant Professor of Medicine, University of Miami School of Medicine; William Bernstein, Associate Attending Physician, Mt. Sinai Hospital; Robert Litwak, Assistant Professor of Surgery; Leonard Silverman, Research Fellow in Cardiology, University of Miami School of Medicine; Hyman Turkewitz, Resident in Medicine; and Milton Lesser, Clinical Assistant in Medicine, Mt. Sinai Hospital, Miami Beach, Florida

Questions and discussion from the floor

Friday, May 31

2:00 p.m.—Scientific Session No. II

Forum on Basic Research in Diseases of the Chest: Cardiac

A Simple Test of Congestive Heart Failure Utilizing the Mass Spectrometer

Richard S. Cosby, Associate Professor of Medicine; Ellery C. Stowell, Ph.D.; Ray Hartwig, A.B.; Robert Thompson, A.B.; and Mary Mayo, B.A., Research Assistants, University of Southern California School of Medicine, Los Angeles, Calif.

A Disposable, Self-Contained, Plastic Sheet Oxygenator for Open Heart Surgery

C. Walton Lillehei, Professor of Surgery; Vincent L. Gott, National Heart Trainee; Richard A. DeWall, Research Fellow, American Heart Association; Robert D. Sellers, Medical Fellow in Surgery; and Richard L. Varco, Professor of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

Experimental Coronary Artery Occlusion: Ventricular Fibrillation and Survival as Affected by Selected Drugs and Ionic Alterations

William T. Williams, Assistant Professor of Surgery; Albert L. Meena, Resident, Department of Surgery; J. D. Hardy, Professor and Chairman, Department of Surgery; and M. D. Turner, Assistant Professor of Research Surgery and Physiology, University of Mississippi Medical Center, Jackson, Mississippi

The Results of Open Heart Surgery with Induced Cardiac Arrest by Potassium Citrate in Patients with Congenital and Acquired Heart Disease

F. Mason Sones Jr., Director, Heart Catheterization Laboratory, Department of Cardiovascular Disease, The Cleveland Clinic, Cleveland, Ohio

Transvalvular Polyvinyl (Ivalon Sponge) Prosthesis for Correction of Mitral Insufficiency

William R. Rumel, Chief, and P. R. Cutler, Division of Thoracic and Cardiovascular Surgery, Latter-Day Saints Hospital, Salt Lake City, Utah

Studies in Vascular Elasticity in Hypertensive Patients

Robert L. Grissom, Professor and Chairman, and Charles A. Hamilton, USPHS Research Fellow, Department of Internal Medicine, University of Nebraska College of Medicine, Omaha, Nebraska

A Study of Myocardial Infarction in Males: An Analysis of 631 Cases

Owen W. Beard, Associate Professor of Medicine; Harold R. Hipp, Associate Professor of Medicine; Richard V. Ebert, Professor and Head, Department of Medicine; James S. Taylor, Associate Professor of Medicine, University of Arkansas School of Medicine, Little Rock; and Morton Robins, Acting Director, Reports and Statistics Service, Veterans Administration, Washington, D. C.

Glycogen Storage Disease of the Myocardium

William F. Mazzitello, Assistant Professor of Medicine; and John F. Briggs, Associate Professor of Clinical Medicine, University of Minnesota Medical School, St. Paul, Minnesota

Questions and discussion from the floor

Friday, May 31

8:15 p.m.—Scientific Session

"Fireside Conferences"
Subjects and Discussion Leaders

Management of Emphysema

Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

E. A. Gaensler, Associate in Surgery, Harvard Medical School, Boston, Mass.

Cardiac Physiology

Richard Bing, Professor of Medicine, Washington University Medical School, St. Louis, Missouri

Donald E. Gregg, Chief, Department of Cardio-Respiratory Diseases, Walter Reed Army Institute of Research, Washington, D. C.

Treatment of Pneumonias

Winthrop N. Davey, Associate Professor of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan

Carl Muschenheim, Associate Professor of Clinical Medicine, Cornell University Medical College, New York City

Surgery of Lung Tumors

William E. Adams, Raymond Professor of Surgery, University of Chicago Medical School, Chicago, Illinois

Richard H. Overholt, Clinical Professor of Surgery, Tufts College Medical School, Boston, Massachusetts

Bronchoesophagology

Paul H. Holinger, Professor of Bronchoesophagology, University of Illinois College of Medicine, Chicago, Illinois

Chevalier L. Jackson, Professor of Laryngology and Bronchoesophagology, Temple University School of Medicine, Philadelphia, Pennsylvania

Management of the Coronary Patient

Ray W. Kissane, Professor of Medicine in Cardiology, Ohio State University College of Medicine, Columbus, Ohio

Arthur M. Master, Consultant Cardiologist, The Mount Sinai Hospital, New York City

Sarcoidosis: Diagnosis and Management

Robert G. Bloch, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Harold Israel, Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Maurice Sones, Associate Professor of Medicine, Woman's Medical College, Philadelphia, Pennsylvania

Congestive Heart Failure

Benjamin Manchester, Assistant Clinical Professor of Medicine, George Washington University School of Medicine, Washington, D. C.

John J. Sampson, Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Inoperable Carcinoma of the Lung

Edgar Mayer, Clinical Professor of Medicine, New York University Postgraduate Medical Center, New York City

A. H. Russakoff, Associate Professor of Clinical Medicine, Medical College of Alabama, Birmingham, Alabama

Fireside Conferences (continued)

Aerosol Therapy

Max S. Sadove, Professor of Surgery (Anesthesiology), University of Illinois College of Medicine, Chicago, Illinois

Maurice S. Segal, Clinical Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts

Peter A. Theodos, Associate in Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

Surgery of the Coronary Artery

Claude S. Beck, Professor of Cardiovascular Surgery, Western Reserve University, University Hospitals, Cleveland, Ohio

David Sabiston, Assistant Professor of Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland

Present Status of IPPB

Roy F. Goddard, Director, Pediatric Research Department, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico

Reginald H. Smart, Clinical Professor of Medicine, Coordinator of Chest Diseases, Consultant, Cardio-Respiratory Laboratory, University of Southern California School of Medicine, Los Angeles, California

Fungus Infections

Joseph W. Peabody, Jr., Instructor in Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

John H. Seabury, Professor of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana

Chemotherapy of Tuberculosis

William R. Barclay, Associate Professor, Department of Medicine, University of Chicago Clinics, Chicago, Illinois

Edward H. Robitzek, Director, Medical Service, Sea View Hospital, Staten Island, New York

Cytologic Diagnosis of Lung Disease

Seymour M. Farber, In Charge, University of California Tuberculosis and Chest Service, San Francisco, California

Edith E. Sproul, Associate Professor of Pathology, Columbia University College of Physicians and Surgeons, New York City

Surgery of Heart Valves

Ralph A. Deterling, Associate Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons, New York City

Dwight E. Harken, Associate Clinical Professor of Surgery, Harvard Medical School, Boston, Massachusetts

Asthma

Ethan Allen Brown, Physician-in-Chief, Allergy Section, Boston Dispensary Unit, New England Medical Center, Boston, Massachusetts

Leon Unger, Associate Professor of Medicine, Northwestern University Medical School, Chicago, Illinois

Surgery in Pulmonary Tuberculosis

Otto C. Brantigan, Professor of Clinical Surgery, Thoracic Surgery, and Surgical Anatomy, University of Maryland School of Medicine, Baltimore, Maryland

Norman Wilson, Assistant Clinical Professor of Surgery, Tufts Medical School, Boston, Massachusetts

BCG Vaccination and Immunity

Sol Rosenthal, Associate Professor, Department of Preventive Medicine, University of Illinois College of Medicine, Chicago, Illinois

Saul Starr, Clinical Associate Professor of Pediatrics, State University of New York College of Medicine, Brooklyn, New York

Fireside Conferences (continued)

Cor Pulmonale

George R. Herrmann, Professor of Medicine, Director, Cardiovascular Service, University of Texas, Galveston, Texas

Irving Mack, Clinical Assistant Professor of Medicine, Chicago Medical School, Chicago, Illinois

Use of Steroids in Pulmonary Diseases

David B. Radner, Director, Chest Department, Michael Reese Hospital, Chicago, Illinois

Harold G. Trimble, Associate Clinical Professor of Medicine, Stanford University School of Medicine, Oakland, California

Tuberculosis in Infants and Children

Arthur W. Dahlstrom, Field Director, New Mexico Tuberculosis Study, Albuquerque, New Mexico

Milton I. Levine, Associate Professor of Pediatrics, Cornell University Medical School, New York City

Bronchiectasis

Earle B. Kay, Chief, Thoracic Surgery, St. Vincent Charity Hospital, Cleveland, Ohio

George S. McReynolds, Associate Professor of Otolaryngology, University of Texas Medical Branch, Galveston, Texas

Pathology of Resected Lesions

David M. Spain, Associate Professor of Pathology, Columbia University College of Physicians and Surgeons, New York City

David H. Waterman, Chief, Thoracic Surgery, Fort Sanders Presbyterian Hospital, Knoxville, Tennessee

Occupational Diseases of the Chest

Harry E. Tebrock, Associate Clinical Professor, Institute of Occupational Medicine, New York University Medical School and Bellevue Hospital, New York City

John H. Weidner, Engineering Laboratory, Ford Motor Company, Dearborn, Mich.

Clinical Pulmonary Physiology

Ernest Attinger, Research Associate, Lung Station (Tufts) and Department of Inhalation Therapy, Boston City Hospital, Boston, Massachusetts

George G. Ornstein, Professor of Medicine, New York Polyclinic Hospital Medical School, New York City

Surgery of Congenital Heart Disease

F. Henry Ellis, Jr., Assistant Professor of Surgery, Graduate Faculty, University of Minnesota Medical School, Rochester, Minnesota

Karl P. Klassen, Professor of Surgery and Chief, Thoracic Surgery Service, Ohio State University College of Medicine, Columbus, Ohio

Home Treatment of Tuberculosis

Ezra V. Bridge, Medical Director and Superintendent, Mineral Springs Sanatorium, Cannon Falls, Minnesota

Irving J. Selikoff, Associate Attending Physician for Thoracic Diseases, The Mount Sinai Hospital, New York City

Management of Chest Injuries

Emil A. Naclerio, Chief Thoracic Surgeon, Harlem Hospital, New York City

Lawrence M. Shefts, Associate Professor of Surgery (Thoracic), University of Texas Medical School, San Antonio, Texas

Pericarditis

Nathaniel E. Reich, Assistant Professor of Clinical Medicine, State University of New York College of Medicine, Brooklyn, New York

Travis Winsor, Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

Clinical Pediatric Cardiology

Robert A. Miller, Head Cardiologist, Children's Memorial Hospital, Chicago, Ill.

Saul J. Robinson, Associate Clinical Professor of Pediatrics, Stanford University School of Medicine, San Francisco, California

Saturday, June 1

10:00 a.m.—Scientific Session No. I

Clinical X-ray Conference

Moderator:

Leo G. Rigler, Professor and Chief, Department of Radiology, University of Minnesota Medical School, Minneapolis, Minnesota

Panel:

Lyman A. Brewer III, Associate Professor of Surgery, College of Medical Evangelists, Los Angeles, California

Coleman B. Rabin, Attending Physician for Chest Diseases, Mt. Sinai Hospital, New York City

Marvin S. Harris, Clinical Professor of Thoracic Diseases, College of Medical Evangelists, Los Angeles, California

Questions and discussion from the floor

10:00 a.m.—Scientific Session No. II

Symposium on Pulmonary Function

Moderator:

Theodore H. Noehren, Assistant Professor of Internal Medicine, University of Buffalo School of Medicine, Buffalo, New York

The Work of Breathing

Richard L. Riley, Associate Professor of Environmental Medicine, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland

Compliance and Resistance

Joseph F. Tomashefski, Chief of Research and Director, Cardio-Pulmonary Laboratory, Ohio Tuberculosis Hospital, Columbus, Ohio

Respiratory Acidosis

R. Drew Miller, Instructor in Medicine, University of Minnesota Graduate Medical School, Rochester, Minnesota

Evaluation of Pulmonary Function Testing

Hurley L. Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California, Los Angeles, California

Questions and discussion from the floor

12:00 noon—Round Table Luncheon Discussions (see Page 365)

2:00 p.m.—Scientific Session

Endarterectomy for Coronary Atherosclerosis

Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Pulmonic Valvular Stenosis Associated with Interatrial Septal Defects

J. L. Ehrenhaft, Professor of Surgery and Chairman, Division of Thoracic Surgery; E. O. Theilen, Assistant Professor, Department of Medicine; Montague S. Lawrence, Research Assistant Professor, Department of Surgery, State University of Iowa School of Medicine, Iowa City, Iowa

Results of Surgical Treatment of Tetralogy of Fallot

(Report of the Committee on Cardiovascular Surgery)

William R. Rumel, Chief, Division of Thoracic and Cardiovascular Surgery, Latter-Day Saints Hospital, Salt Lake City, Utah

Clinical Features and New Method of Management of "Mild" Myocardial Infarction

Myron Prinzmetal, Associate Professor of Clinical Medicine, University of California School of Medicine; Stanley M. Weiner and Mannish Bhuyan, Research Fellows, Los Angeles County Heart Association, Los Angeles, California

Aspiration Pneumonia

Harold A. Lyons, Associate Professor of Medicine; and Irvin H. Besman, Assistant Instructor in Medicine, State University of New York College of Medicine, Brooklyn, New York

Physiologic Criteria for Resectional Surgery in Emphysema

Roger H. L. Wilson, Assistant Clinical Professor of Medicine; Orville F. Grimes, Assistant Professor of Surgery; Seymour M. Farber, Associate Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Questions and discussion from the floor

Sunday, June 2

9:00 a.m.—Scientific Session No. I

Symposium on the Hazards of Nuclear Energy

Moderator:

George R. Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, and Chief, Radioisotope Service, Thayer Veterans Administration Hospital, Nashville, Tennessee

Inhalation Hazards in Nuclear Energy Programs: Stable Elements

Gerritt W. Schepers, Director, Saranac Laboratory, Saranac Lake, New York

The Program of the Atomic Energy Commission for Control of Inhalation Hazards of Nuclear Reactors

Charles L. Dunham, Chief, Division of Biology and Medicine, Atomic Energy Commission, Washington, D. C.

The Public Health Aspect of Nuclear Energy with Particular Reference to Inhalation Hazards and to Diseases of the Chest

Albert L. Chapman, Chief, Division of Special Health Services, Department of Health, Education and Welfare, Public Health Service, Washington, D. C.

Questions and discussion from the floor

10:30 a.m.—Scientific Session

What the Chest Physician Should Know About Radiation Hazards

Richard H. Chamberlain, Professor of Radiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Surgery of the Definable X-Ray Lesion in Apparently Healthy Military Personnel

Lt. Norman Cooley, General Surgery Resident; Capt. J. M. Hanner, Chief of Surgery; Capt. Edgar Ricen, Chief, Medical Chest Service; and Cdr. Ivan D. Baronofsky, Head of Section, Thoracic Surgery, U. S. Naval Hospital, San Diego, California

The Treatment of Spontaneous Pneumothorax with Kaolin

G. H. C. Joynt, Clinical Teacher; and R. C. Laird, Associate Professor of Surgery, University of Toronto Faculty of Medicine, Toronto, Canada

9:00 a.m.—Scientific Session No. II

Symposium on Congenital Heart Disease

Diagnosis of Atrial Septal Defects

S. Gilbert Blount, Associate Professor of Medicine and Head, Section of Cardiology, University of Colorado School of Medicine, Denver, Colorado

Aortic Stenosis

Daniel F. Downing, Associate Professor of Pediatrics, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Diagnosis of Ventricular Septal Defects

Mary Allen Engle, Assistant Professor of Pediatrics, Cornell University Medical College, New York City

Cardiac Hypertrophies Without Shunts

Sidney Blumenthal, Assistant Clinical Professor of Pediatrics, Columbia University College of Physicians and Surgeons, New York City

The Natural Transformation of Ventricular Septal Defects into Ventricular Septal Defects with Pulmonary Stenosis and/or into the Noncyanotic Type of Tetralogy of Fallot—New Clinical and Physiologic Findings

Benjamin M. Gasul, Director, Pediatric Cardiophysiology Department, Cook County Children's Hospital and Hektoen Institute for Medical Research; Robert F. Dillon, Cardiophysiologist; and Vlastimil Vrla, Fellow, Pediatric Cardiology, Cook County Children's Hospital, Chicago, Illinois

Indications for Surgical Intervention in Congenital Malformations of the Heart

Panel Discussion

Moderator:

Egbert H. Fell, Clinical Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois

Panel:

Janet S. Baldwin, Associate Professor of Pediatrics, New York University College of Medicine, New York City

James W. DuShane, Assistant Professor of Pediatrics, University of Minnesota Graduate School of Medicine, Rochester, Minnesota

C. Walton Lillehei, Professor of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

Robert F. Ziegler, Physician-in-Charge, Division of Pediatric Cardiology, Henry Ford Hospital, Detroit, Michigan

Questions and discussion from the floor

12:00 noon—Round Table Luncheon Discussion (see Page 366)

2:00 p.m.—Scientific Session

Experiences With Myocardial Revascularization by Division of the Internal Mammary Arteries

Robert P. Glover, Director of Cardiovascular Research Laboratories and Chief of Thoracic and Cardiac Surgery, Presbyterian Hospital; J. Roderick Kitchell, Assistant Professor of Medicine, Graduate School of Medicine, University of Pennsylvania; and Julio C. Davila, Associate Director, Thoracic and Cardiovascular Research Laboratories, Presbyterian Hospital, Philadelphia, Pennsylvania

An Aerosol Method of Producing and Collecting Bronchial Secretions in Normal Subjects: Its Use as a Clinical Technique for Lung Cancer

Hylan A. Bickerman, Assistant Clinical Professor of Medicine; and Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

The Decreasing Hazard of Surgical Procedures on Patients with Asthma

Louis E. Prickman, Associate Professor of Medicine; and Fred F. Whitcomb, Jr., Fellow in Medicine, Mayo Foundation, University of Minnesota Medical School, Rochester, Minnesota

Recent Advances in Bronchography

John E. Rayl, Assistant Chief, Surgical Service; and Daniel E. Smith, Chief of Bronchoesophagology Division, Veterans Administration Hospital, Oteen, North Carolina

Bronchography—Summary of a World Wide Survey

(Report of the Committee on Bronchoesophagology)

Arthur M. Olsen, Associate Professor of Medicine, Mayo Foundation, University of Minnesota Medical School, Rochester, Minnesota

Experiences in the Therapy of Sixty Cases of Deep Mycotic Infections

Patrick Lehan, Public Health Service; Charles A. Brasher, Superintendent, Missouri State Sanatorium; Louis Yates, Chief, Medical Service, Missouri State Sanatorium, Mt. Vernon; and Michael Furcolow, Associate Clinical Professor of Medicine, University of Kansas Medical Center, Kansas City, Kansas

Clinical Application of Pulmonary Diffusing Capacity Measurements

Edward A. Gaensler, Associate in Surgery, Harvard Medical School; David W. Cugell, Associate in Medicine and Director, Cardiopulmonary Laboratory, Northwestern University Medical School, Chicago; Asher Marks, Director, Cardiopulmonary Laboratory, Jackson Memorial Hospital, Miami; and John B. Cadigan, Assistant in Medicine, Harvard Medical School, Boston, Massachusetts

Questions and discussion from the floor

ROUND TABLE LUNCHEONS

Friday, May 31

A-1 ***Surgical Treatment of Coronary Artery Disease***

Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Victor P. Satinsky, Director of Cardiovascular Research, Temple Hospital, Los Angeles, California

Franklin R. Smith, Clinical Associate in Surgery, University of Washington School of Medicine, Seattle, Washington

Moderator: **Charles A. Hufnagel**, Associate Professor of Surgery, Professor of Surgical Research, and Director of the Experimental Laboratory, Georgetown University Medical Center, Washington, D. C.

A-2 ***Rheumatic Fever***

Banice Feinberg, Physician-in-Chief, Department of Pediatrics, Rhode Island Hospital, Providence, Rhode Island

Raphael N. Paul, Director, Children's Heart Clinic, John Gaston Hospital, Memphis, Tennessee

Robert A. Tidwell, Director of Cardiology, Children's Orthopedic Hospital, Seattle, Washington

Moderator: **Donald E. Cassels**, Associate Professor of Pediatrics, University of Chicago School of Medicine, Chicago, Illinois

A-3 ***Problem of Recent Tuberculin Converters***

Albert R. Allen, Medical Director and Superintendent, Central Washington Tuberculosis Hospital, Selah, Washington

J. Arthur Myers, Professor of Internal Medicine and Public Health, Medical and Graduate Schools, University of Minnesota, Minneapolis, Minnesota

Robert L. Yeager, Medical Director, Summit Park Sanatorium, Pomona, New York

Moderator: **W. Leonard Howard**, Superintendent, William H. Maybury Sanatorium, Northville, Michigan

A-4 ***Psychosomatic Aspects of Pulmonary Disease***

Sidney H. Dressler, Medical Director, National Jewish Hospital, Denver, Colo.

Thomas H. Holmes, Associate Professor of Psychiatry, University of Washington School of Medicine, Seattle, Washington

Emil Rothstein, Chief, Tuberculosis Service, Veterans Administration Hospital, Brockton, Massachusetts

Moderator: **P. J. Sparer**, Professor of Psychiatry and Preventive Medicine, University of Tennessee College of Medicine, Memphis, Tennessee

A-5 ***Bronchopulmonary Suppuration—Medical and Surgical Management***

Norman Arcese, Clinical Associate in Medicine, University of Washington School of Medicine, Seattle, Washington

John S. Harter, Assistant Professor of Surgery, University of Louisville School of Medicine, Louisville, Kentucky

Henry J. Stanford, Thoracic Surgeon, Tucson Medical Center Hospital, Tucson, Arizona

Moderator: **Albert H. Andrews**, Associate Clinical Professor of Bronchoesophagology, University of Illinois College of Medicine, Chicago, Illinois

A-6 ***Allergy as a Factor in Pulmonary Disease***

Murray Dworetzky, Assistant Professor of Clinical Medicine, Cornell Medical College, New York City

Merle W. Moore, Associate Clinical Professor of Medicine and Head, Division of Allergy, University of Oregon Medical School, Portland, Oregon

Orval R. Withers, Head, Allergy Clinic, University of Kansas Medical Center, Kansas City, Missouri

Moderator: **Bret Ratner**, Professor of Clinical Pediatrics and Director of Pediatric Allergy, New York Medical College, New York City

Round Table Luncheons

Saturday, June 1

S-1 *Open Heart Surgery*

Edward M. Kent, Associate Professor of Surgery and Head, Department of Thoracic Surgery, University of Pittsburgh School of Medicine, Pittsburgh, Pa.

Conrad R. Lam, Surgeon-in-Charge, Division of Thoracic Surgery, Henry Ford Hospital, Detroit, Michigan

Arthur Vineberg, Lecturer-in-Surgery, McGill University Faculty of Medicine, Montreal, Canada

Moderator: **F. Mason Sones, Jr.**, Director, Heart Catheterization Laboratory, The Cleveland Clinic, Cleveland, Ohio

S-2 *Coronary Disease*

E. Grey Dimond, Professor of Medicine and Chairman, Department of Medicine, and Director, Cardiovascular Laboratory, University of Kansas Medical Center, Kansas City, Kansas

William Likoff, Associate Professor of Medicine, Hahnemann Medical College, Philadelphia, Pennsylvania

Myron Prinzmetal, Associate Professor of Clinical Medicine, University of California School of Medicine, Los Angeles, California

Moderator: **Oglesby Paul**, Clinical Associate Professor of Medicine, University of Illinois College of Medicine, Chicago, Illinois

S-3 *Chemotherapy in Tuberculosis*

Edward Dunner, Secretary, Committee on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C.

Robert A. Goodwin, Associate Professor of Clinical Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

John K. Lattimer, Professor of Urology, Columbia University College of Physicians and Surgeons, New York City

Moderator: **Alfred S. Dooneief**, Attending Physician, Montefiore Hospital, New York City

S-4 *Nontuberculous Pulmonary Diseases*

M. Eugene Flipse, Associate Professor of Medicine and Chief, Chest Section, University of Miami School of Medicine, Miami, Florida

Joseph E. Geraci, Assistant Professor of Medicine, Mayo Clinic and University of Minnesota Graduate School of Medicine, Rochester, Minnesota

William Lester, Chief of Staff, Suburban Cook County Tuberculosis Sanitarium District, Hinsdale, Illinois

Moderator: **Sol Katz**, Chief, Pulmonary Disease Division, District of Columbia General Hospital, Washington, D. C.

S-5 *Pulmonary Mycoses*

Alvis E. Greer, Clinical Professor of Medicine, Baylor University College of Medicine, Houston, Texas

Patrick Lehan, Public Health Service, Kansas City, Kansas

Harry E. Walkup, Chief, Surgical Service, Veterans Administration Hospital, Oteen, North Carolina

Moderator: **Arthur Q. Penta**, Visiting Lecturer, Temple University Medical School (Philadelphia), Schenectady, New York

S-6 *Occupational Diseases of the Lungs*

Daniel C. Braun, Medical Director, Industrial Hygiene Foundation, Pittsburgh, Pennsylvania

Frank Princi, Associate Professor of Industrial Medicine, University of Cincinnati, School of Medicine, Cincinnati, Ohio

Israel Rappaport, Associate Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons, New York City

Moderator: **H. S. Van Ordstrand**, Professor of Pulmonary Diseases, Frank E. Bunts Education Institute of the Cleveland Clinic Foundation, Cleveland, Ohio

Round Table Luncheons

Sunday, June 2

C-1 ***Hypertension***

David Gelfand, Assistant Professor of Cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Maurice Schnitker, Director of Medicine and Chief, Medical Service, St. Vincent's Hospital, Toledo, Ohio

Col. Weldon J. Walker, Chief, Cardiovascular Service, Brooke Army Hospital, Fort Sam Houston, Texas

Moderator: **Robert L. Grissom**, Professor and Chairman, Department of Internal Medicine, University of Nebraska School of Medicine, Omaha, Neb.

C-2 ***Clinical Aspects of Pulmonary Function Testing***

Ross Kory, Chief, Investigative Medicine (Research) and Assistant Chief, Medical Service, Veterans Administration Hospital, Wood, Wisconsin

Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago, Illinois

Roger H. L. Wilson, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

Moderator: **Howard G. Dayman**, Assistant Professor of Medicine, University of Buffalo School of Medicine, Buffalo, New York

C-3 ***Surgery in Lung Cancer—Present Status***

DeWitt C. Daughtry, Assistant Clinical Professor of Surgery, University of Miami School of Medicine, Miami, Florida

Alfred Goldman, Co-Chairman, Department of Surgery, City of Hope Medical Center, Los Angeles, California

Coleman B. Rabin, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Moderator: **Herbert C. Maier**, Director of Surgery, Lenox Hill Hospital, New York City

C-4 ***"Open Negative" Cases: To Resect or Not to Resect***

Oscar Auerbach, Chief, Laboratory Service, Veterans Administration Hospital, East Orange, New Jersey

Harry L. Katz, Chief, Chest Section, Veterans Administration Hospital, Brooklyn, New York

Robert R. Shaw, Clinical Professor of Surgery, Southwestern Medical College, Dallas, Texas

Moderator: **Roger S. Mitchell**, Director, Colorado Foundation for Research in Tuberculosis, Denver, Colorado

C-5 ***Appraisal of Mass X-Ray Surveys***

Robert J. Anderson, Medical Director and Chief, Communicable Disease Center, Public Health Service, Atlanta, Georgia

Katharine R. Boucot, Professor of Preventive Medicine and Clinical Professor of Medicine, Woman's Medical College, Philadelphia, Pennsylvania

Clarence M. Sharp, Director, Bureau of Preventable Diseases, Florida State Board of Health, Jacksonville, Florida

Moderator: **J. P. Medelman**, Clinical Associate Professor of Radiology, University of Minnesota Medical School, St. Paul, Minnesota

C-6 ***Collagen Diseases of the Lungs***

Andrew L. Banyai, Associate Clinical Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

Alfred Goldman, Associate Professor of Clinical Medicine and Director, Medical Chest Clinic, Washington University School of Medicine, St. Louis, Missouri

David M. Gould, Professor and Chairman, Department of Radiology, University of Arkansas Medical Center, Little Rock, Arkansas

Moderator: **Eli H. Rubin**, Professor of Clinical Medicine, Albert Einstein College of Medicine, Yeshiva University, New York City

MOTION PICTURE PROGRAM

The following is a portion of the program of motion pictures dealing with diseases of the chest to be shown concurrently with the scientific program on the three days of the meeting, Friday, Saturday and Sunday, May 31, June 1 and June 2. Additional films are being considered by the Committee on Motion Pictures of the College for presentation.

Resection with Homograft Replacement of Thoraco-Abdominal Aneurysm of Aorta Involving Celiac Superior and Renal Arteries

Michael E. DeBakey, Baylor University College of Medicine, Houston, Texas

Radical Pneumonectomy with Intrapericardial Dissection

F. Henry Ellis Jr., Mayo Clinic, Rochester, Minnesota

New Developments in Bronchoscopic Photography and Cinematography, Including Adaptation for Television

J. M. Dubois de Montreynaud and R. J. Edwards, Regional Cancer Center, Reims, France

Surgical Treatment of Coronary Artery Disease

Claude S. Beck and David Leighninger, University Hospitals, Cleveland, Ohio

Surgical Excision of Post Infarction Ventricular Aneurysm

Edward E. Avery, Thomas Shields, Robert Hohf, Victor Bernhard and Craig Borden, Veterans Administration Research Hospital, Chicago, Illinois

Mediastinal Exploration for Parathyroid Adenoma

O. Theron Clagett, Mayo Clinic, Rochester, Minnesota

Glossopharyngeal Breathing

C. W. Dail and J. Affeldt, Rancho Los Amigos Respiratory Center for Polio, Hondo, California (National Foundation for Infantile Paralysis, New York City)

SOCIAL ACTIVITIES

Saturday, June 1

6:00 p.m.—Annual Convocation (Formal)

7:00 p.m.—Cocktail Party
Sponsored by The Panray Corp., New York City

7:30 p.m.—Annual Presidents' Banquet

8:30 p.m.—After-Dinner Dancing

The above functions will be held at the Hotel Commodore

Annual Meeting

NEW YORK STATE CHAPTER

Wednesday, May 29, Hotel Commodore

6:00 p.m.—Dinner
Ida Levine, Brooklyn, Chapter President, Presiding

ANNUAL HOWARD K. LILIENTHAL LECTURE

Chronic Bronchitis and Emphysema of the Aged

Edgar Mayer, Clinical Professor of Medicine, New York University Graduate School of Medicine, New York City

ADMINISTRATIVE SESSIONS

Wednesday, May 29

8:00 a.m.—Committee on Seminars

10:00 a.m.—Executive Council

2:00 p.m.—Board of Regents

3:30 p.m.—Teaching Seminar, Council on Undergraduate Medical Education

4:00 p.m.—Council on Hospitals and Special Committee of the Board of Regents

Thursday, May 30

9:00 a.m.—Joint Meeting, Board of Governors and Board of Regents

9:00 a.m.—Council and Committee Meetings

- Council on Undergraduate Medical Education
- Committee on Undergraduate Medical Education
- Committee on Motion Pictures
- Committee on Audiovisual Aids
- Committee on College Essay
- Committee on Resident Loan Fund
- Council on Postgraduate Medical Education
- Council on Research
- Committee on Non-Surgical and Drug Therapy
- Committee on Pulmonary Surgery
- Committee on Bronchoesophagology
- Committee on Chemotherapy and Antibiotics
- Committee on Physiologic Therapy
  - Section on Inhalation Therapy
  - Section on Nomenclature in Cardiopulmonary Physiology
- Committee on Allergy
- Committee on Microbiology
- Committee on Pulmonary Diseases in Children
- Committee on Cardiovascular Disease
  - Section on Clinical Cardiovascular Disease
  - Section on Cardiovascular Surgery
  - Section on Cardiovascular Physiology
  - Section on Electrocardiography
  - Section on Rehabilitation
  - Section on Roentgenology
  - Section on Pediatric Cardiology
  - Section on Therapy
- Council on Public Health
- Committee on Indian Affairs
- Committee on Liaison with State and County Medical Societies
- Committee on Occupational Diseases of the Chest
- Council on Hospitals
- Committee on Standards and Accreditation
- Committee on Rehabilitation
- Committee on Chest Diseases in Institutions
- Committee on Psychosomatic Aspects of Diseases of the Chest
- Committee on Resident Fellowships

10:30 a.m.—Committee on Membership

12:00 noon—**LUNCHEON, 13th ANNUAL COLLEGE CONFERENCE**

James H. Stygall, Indianapolis, Indiana, Immediate Past President, American College of Chest Physicians, presiding

Address of the President of the College
Herman J. Moersch, Rochester, Minnesota

Awarding of Certificates of Merit to Past-Presidents of College Chapters

1:30 p.m.—Board of Examiners

2:00 p.m.—Joint Meetings of all Councils and their Committees and Sections

4:00 p.m.—OPEN FORUM, COUNCIL ON HOSPITALS

Challenging Questions Relative to our Tuberculosis Institutions

Charles A. Brasher, Mount Vernon, Missouri, Chairman

Conversion of Tuberculosis Hospitals into Chest Hospitals

Medical Aspects

Samuel Cohen, Director of Medicine, Pollak Hospital For Chest Diseases, Jersey City, New Jersey

Administrative Aspects

Thomas J. Finn, Superintendent, Pollak Hospital for Chest Diseases, Jersey City, New Jersey

Admission of Tuberculous Mental Patients

Andrew L. Banyai, Clinical Director, Muirdale Sanatorium, Milwaukee, Wisconsin

The Viewpoint of the Private Practitioner

Hollis E. Johnson, Visiting Physician and Director of Chest Clinic, Vanderbilt University Hospital, Nashville, Tennessee

To Close or Not to Close Tuberculosis Institutions

J. Arthur Myers, Professor of Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Minneapolis, Minnesota

Questions and discussion from the floor

EXAMINATIONS FOR FELLOWSHIP

9:00 a.m.—Written Examinations

2:00 p.m.—Oral Examinations

Friday, May 31

2:00 p.m.—Committee on Nominations

2:00 p.m.—Committee on Insurance

3:00 p.m.—Editorial Board

5:00 p.m.—Chapter Meetings

Saturday, June 1

9:00 a.m.—OPEN ADMINISTRATIVE SESSION

Report of the Historian
Report of the Treasurer
Report of the Committee on Bylaws
Report of the Executive Director
Report of the Committee on Nominations
Election of Officers

10:00 a.m.—Executive Council

Sunday, June 2

8:00 a.m.—Past-Presidents' Breakfast

10:00 a.m.—Executive Council

2:30 p.m.—Board of Regents

6:00 p.m.—Section on Pediatric Cardiology

TECHNICAL EXHIBITORS

Be sure to visit the Technical Exhibits! There will be intermissions each day to allow you the opportunity of visiting the booths and meeting the sales representatives of our exhibitors.

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George P. Pilling & Son Company
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Puritan Compressed Gas Corporation
Kansas City Missouri and

V. Ray Bennett & Associates, Inc.
Los Angeles, California

W. B. Saunders Company
Philadelphia, Pennsylvania

Schering Corporation
Bloomfield, New Jersey

Charles C Thomas—Publisher
Springfield, Illinois

Winthrop Laboratories
New York, New York

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Urgent Notice

By completing this form and returning it at once to the Executive Offices of the College, you will avoid having to stand in line at the Registration Desk of the annual meeting in New York City. Your badge and program, as well as luncheon, banquet and seminar tickets, will be prepared in advance and will be awaiting your arrival at the Hotel Commodore. Please complete both sides of this Advance Registration Form and mail promptly. Thank you.

Non-members must enclose registration fee of $25.00 with this form.

Please make checks payable to **American College of Chest Physicians**

RESERVATION FORM

Seminars, Wednesday, May 29

$7.50 each for members (Included in $25.00 registration fee for non-members)

Morning Sessions (9 a.m.-12 noon)		Afternoon Sessions (2:00-5:00 p.m.)	
First Choice	A.M.....	First Choice	A.M.....
Second Choice	A.M.....	Second Choice	A.M.....

Please indicate choice by number as listed in program

Round Table Luncheons ***$5.00 each***

	Friday, May 31	Saturday, June 1	Sunday, June 2
First Choice	A-.....	B-.....	C-.....
Second Choice	A-.....	B-.....	C-.....
Third Choice	A-.....	B-.....	C-.....

Please indicate choice by number as listed in program

Luncheon, 13th Annual College Conference ***$5.00 each***
Thursday, May 30

I wish to reserve.....tickets for the Annual College Conference to be held on Thursday noon, May 30.

PRESIDENTS' BANQUET
Saturday, June 1, Hotel Commodore
New York City

Cocktails—Dinner—Dancing ***Tickets: $9.75 each***

All places at the Annual Presidents' Banquet are reserved. Tables will be assigned in order of requests received. Please order your tickets at once so that you may be assigned your table early. Tables for ten may be reserved upon receipt of payment for tickets and names of persons in the party. This is the gala College evening of the year and you will not want to miss it!

I wish to reserve.....tickets for the Annual Presidents' Banquet, Saturday, June 1, 7:00 p.m. (price includes cocktails, dinner and dancing.)

Please complete coupon on reverse side

NOTE: Make checks payable to *American College of Chest Physicians*. Checks must accompany all requests for reservations and will be accepted in the order in which they are received. All tickets will be held for pick-up at the College Registration Desk, Hotel Commodore.

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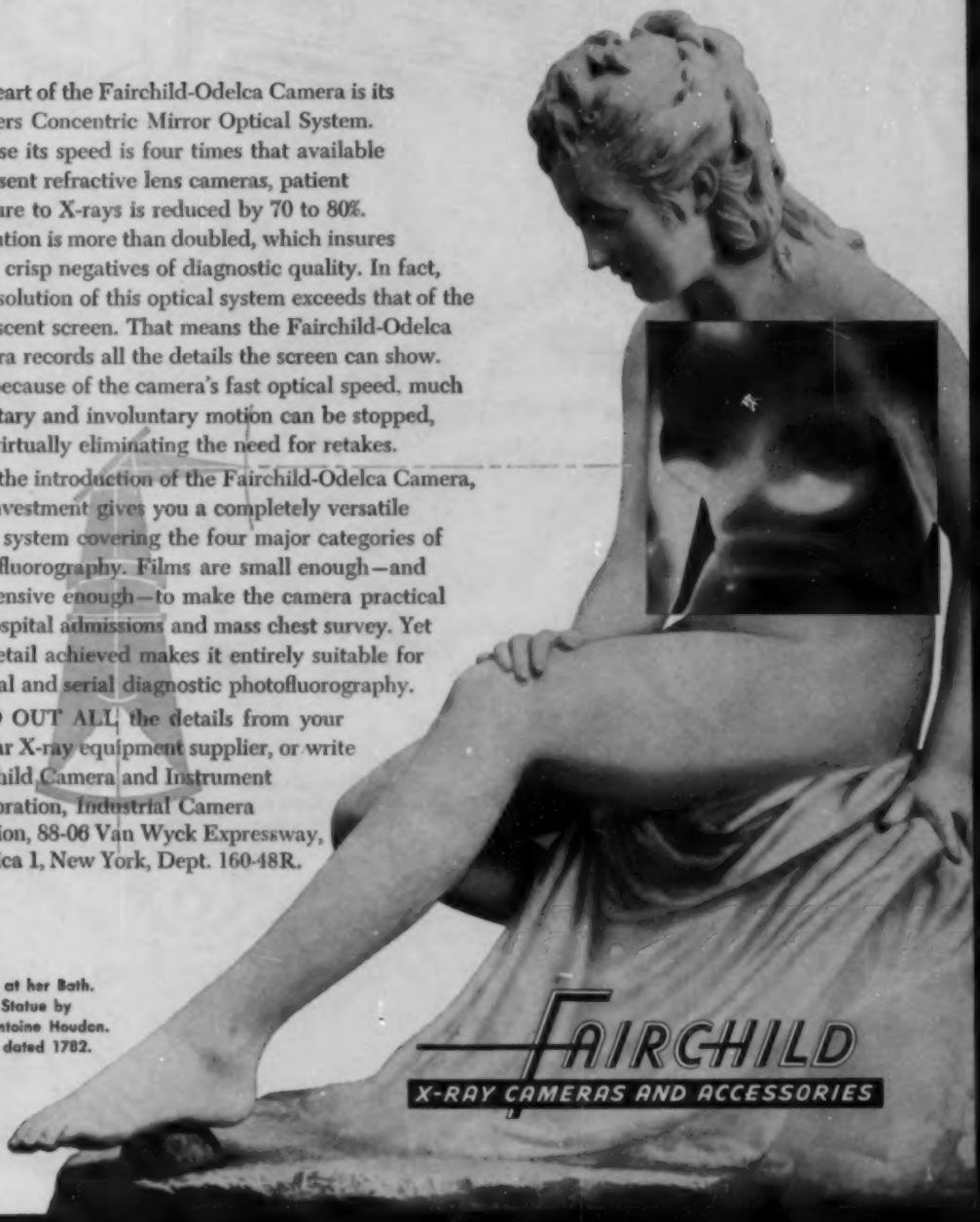

Woman at her Bath. Marble Statue by Jean Antoine Houdon. French, dated 1782.

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